GROWTH

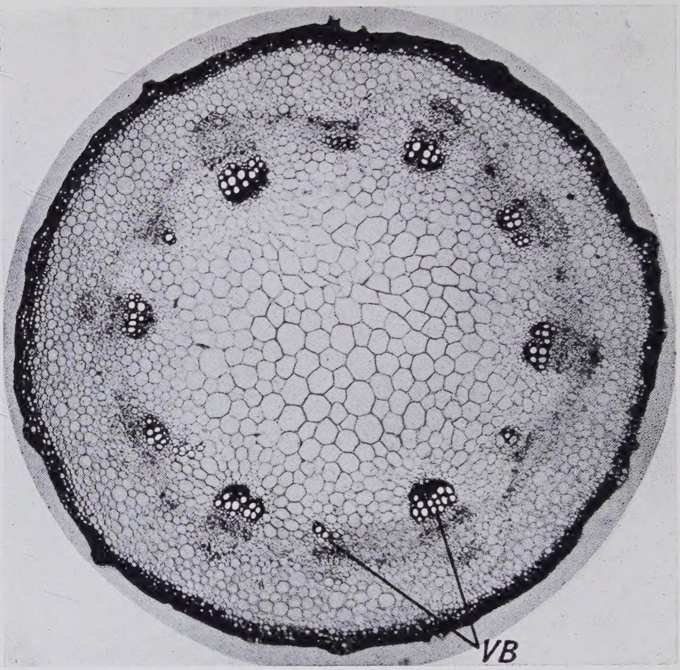

FIG. 1.—A transverse section of a stem of a young dicotyledonous plant before secondary growth in thickness has occurred. *VB* = vascular bundles.

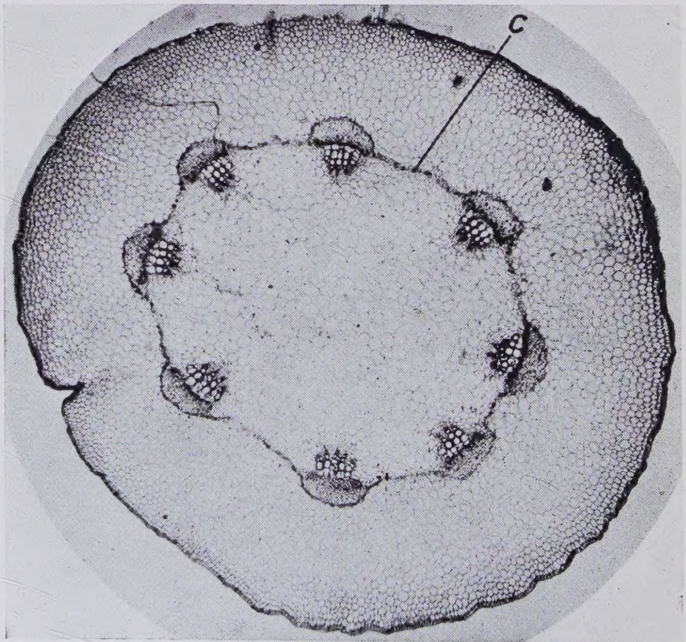

FIG. 2.—A similar stem after growth in thickness has started. The cambium ring (*C*) is now continuous.

GROWTH

BY

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To

MY FATHER AND MOTHER

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PREFACE

In preparing this little work on Growth I have attempted to keep the general aspect of the problem in view the whole time. It is a subject in which there is much scope for specialization, but the general biological point of view should not be lost in an elementary presentation of the subject. As it is impossible to appreciate Growth proper without a few biological principles, an irreducible minimum of these has been worked in.

In spite of the fact that Growth is a phenomenon of such universal occurrence and importance, practically nothing was known about it until the introduction of the experimental method, quite recently. The study is still in its infancy, which must account for, although it does not excuse, the lack of cohesion in the presentation. The main theme around which the book is written is that growth is a fundamental property of living matter, and that it takes place whenever circumstances do not prevent it.

I have simplified the language and the subject-matter as far as possible without depriving the recorded experiments and observations of their significance, and hope thereby to have made my account easily intelligible. All technical terms have been eliminated with the exception of a very few, which, being indispensable, are retained with a complete explanation.

The accounts of the various observations and experiments have for the major part been drawn from the original papers and journals in which they appeared. References to the more recent of these and to such as have not yet had time to find their way into bibliographies will be found

in the Appendix at the end of the book. At the same time, as this list will only appeal to the specialist, I have placed at the end of each chapter a short list of the more recent standard books bearing on the subject of the chapter, for the use of those who wish to follow up the subjects to which this book is merely an introduction.

It remains for me to express my deep gratitude to my friend Mr. Julian Huxley for reading parts of the MS. and making many helpful criticisms and suggestions. To Mr. R. Snow, of Magdalen College, I am indebted for guidance in certain botanical matters where I was apt to go astray. To Mr. C. S. Elton I owe some suggestions for Chapter XI. Most of the figures have been specially drawn for this book, and I am indebted to Mr. Kempin for some botanical preparations and to Mr. Chesterman for assistance with photographs. For the rest, my gratitude is due to Dr. Knud Sand for his photographs of the rejuvenated dog, to Dr. Drew for his drawings of tissue cultures, to Dr. Church for his phyllotaxis figures, to Dr. Allen and Dr. Champy for permission to copy parts of drawings, and to the Editors of the *Quarterly Journal of Microscopical Science*, the *Quarterly Journal of Experimental Physiology* and of the *School Science Review*, and to the Cambridge University Press for permission to reproduce figures.

G. R. de B.

OXFORD, 1924.

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CHAPTER I

INTRODUCTION

This book attempts to show what Growth is, what it does and how it does it.

The process of growing implies getting bigger, and this increase in size is what should strictly be termed growth. Its effects are often very striking when young animals (or plants) are compared with their adults, and sometimes give rise to the impression that development is nothing more than spatial enlargement. The most familiar developing organisms (a word meaning living things), such as children, kittens, puppies or chicks are born or hatched as more or less perfect minute editions of their parents. If the problem stopped there it would be comparatively simple, but it does not. Consider the egg of a hen, and, by the way, the object which is boiled and eaten for breakfast is more than an egg, for it also consists of a layer of albumen (white) and a shell. The true egg or ovum is only that which is contained inside the membrane that just surrounds the yolk. Now this ovum bears no resemblance whatever to a hen. It is a spherical object and if it were merely to get larger it would still be of a spherical shape, and not a hen.

Clearly then, growth alone cannot be responsible for the processes of development whereby an adult organism is produced from an ovum; something else must be necessary to bring about the result, and this it is which complicates the problem. This second process is really one of moulding and changing of shape, so that out of the simple spherical ovum the complicated adult form is produced.

Since this process results in making the various parts of the organism different from one another, it is called *differentiation.*

The many processes which constitute development cannot therefore be reduced to one heading but fall naturally into two: there is increase in size, and increase in complexity of structure and shape, or, in other words, growth and differentiation. All living organisms in their life-history from the ovum to the adult are subjected to these two processes. The reason why only growth is visible in the case of developing children, kittens, etc., is that the earlier periods, when differentiation is doing its work, are concealed within the body of the mother or the shell of the egg, and by the time of birth or hatching most of the differentiation has been done and they merely have to grow.

It is necessary now to see why differentiation must be brought in when dealing with growth. The simplest and most obvious method of bringing about a change of shape is for growth to take place more rapidly in some directions than in others. A sphere may be transformed into an oval-shaped structure; by the growth of one layer over another more than one skin may be formed, and by growth outwards from particular spots little cones can be raised which will ultimately become limbs. In fact, differentiation of shape is nothing but a peculiar kind of growth, and as such must be included.

There is another reason which must be considered. As the various parts of an organism differentiate each is able to perform certain tasks which are necessary for the life of the organism. The eye sees, the skeleton supports, the stomach digests, the limbs effect locomotion. The ability to perform these functions necessitates a specialization of the actual substance of the organism so as to render its tissues fit for their various purposes. Muscular tissue differs from skeletal, nervous from glandular as a result of a process of differentiation of tissues, which provides

them with the necessary complexity of structure. The importance of this lies in the fact that only those tissues of a sufficiently low degree of differentiation are capable of growing.

All living organisms are composed of cells, microscopical corpuscles of living matter or protoplasm which are comparable to the bricks of which a house is built. Groups of cells of the same kind form tissues; these make up organs such as the heart or brain and the organs compose the organism. New cells can only arise from cells already existing by a process of division. It is clear that increase in size of an organism may be brought about either by growth of its constituent cells, or by increase in their number through division while their size remains the same. Both possibilities occur, but the latter is by far the more important and is often designated "true" growth. If for any reason cells are unable to divide, true growth is impossible, and this is what happens when they have reached a certain stage of differentiation. For the differentiation of the tissues is nothing but the differentiation of the cells of which they are made up, and as it is useful to have an expression which accurately describes this condition it is called *histological* differentiation. This, then, is to be distinguished from the process of moulding and increasing the complexity of the shape of the whole organism which is called *morphological* differentiation.

Having introduced these two kinds of differentiation and shown the important bearing which they have on growth, it is time to return to growth itself and to notice that it may be brought about in several different ways. It may be due to increase in quantity of living matter and therefore to the production of new protoplasm, as living matter is called. At other times increase in size may be due to the accumulation of substances which are not "living," such as yolk which is stored up inside egg cells. The inorganic salts which constitute bone are another example, and in this case they are deposited outside and

between the cells, from which position they are known as intercellular substances. Lastly, increase in size may be brought about by absorption of water which swells up the organism.

The production of new living matter is due to the building-up of simpler substances into protoplasm, these substances being food, water, oxygen, etc. Protoplasm, which has a chemical constitution so complicated that it has never been analysed, is always undergoing changes in its constitution. The new matter from the food is built up into it and the old is broken down into decomposition products, to be made good by more new matter. These changes in the protoplasm, which are the characteristic of living matter, constitute what is known as *metabolism*, a constant interplay between the constructive and destructive processes. For there to be increase in the quantity of protoplasm, naturally the constructive processes must be in excess of the destructive ones. Now metabolism goes on throughout life, the destructive effects of wear and tear have to be made good and new protoplasm is constantly being built up as long as the organism lives. As this goes on after the organism has ceased growing, it is clear that increase in size by the production of new protoplasm is not a special phenomenon solely connected with growth, but only a special relation of the constructive and destructive processes of metabolism, both of which are fundamental and permanent properties of protoplasm whether growing or not.

In a more or less similar way it can be shown that cell division, which is so important a process in true growth, is not confined to growth. During the time when an organism is growing rapidly it is producing new protoplasm and its cells increase in number by rapid and frequent divisions. But in some cases, a large cell may divide many times and produce smaller cells without there being any increase in quantity of protoplasm. If a piece of paper be cut in two and the pieces cut in two again and

again, there will be a larger number of pieces, but there will be no more paper than there was in the single whole piece. This is what happens at the very beginning of development and shows that cell division is not invariably connected with increase in size.

Again, after an organism has reached the adult condition, repair of waste tissues is brought about by cell division, but the organism undergoes no increase in size, for the same amount is replaced as was lost. It is obvious, therefore, that cell division may occur with or without growth, and is not a peculiar attribute of growth.

It is now becoming clear that growth is no single process, but rather that it is a combination of a great many. Defined as increase in size it covers: production of new protoplasm, accumulation of inert substances like yolk, absorption of water, and also morphological differentiation, since this is only growth in certain definite directions. At the same time, growth does not include the whole of these processes, since they may also occur without growth.

All attempts at making definitions by hard and fast lines are difficult, and especially in biological science, for exceptions are always cropping up so that the rules break down. Unfortunately "increase in size" is a cut-and-dried definition, and consequently it is not a matter for surprise that the processes contributing to it should overlap its limits in an untidy fashion, for they are only certain instances of more general phenomena.

At this stage it will be convenient to draw up the conclusions arrived at in the form of a table which will be easier to refer to and will also help to make clear anything that has hitherto seemed obscure.

Growth is increase in size:

It may be due to:

(I) increase in size of whole organisms,

(II) increase in size of parts of organisms, thereby producing morphological differentiation,

in both cases due to :

(i) increase in size of cells,
(ii) increase in number of cells (true growth),
(iii) increase of intercellular substances,

and caused by

(*a*) production of new protoplasm,
(*b*) accumulation of non-living substances (bone, yolk),
(*c*) absorption of water.

Enough has now been said to show that Growth is not a phenomenon to be taken for granted, but that it is necessary to analyse it very carefully in order to see what is at work, and its constituent processes are many.

CHAPTER II

THE GROWTH OF THE FROG

In order to understand what growth does it is necessary to take some concrete example and to watch it grow during its development. For this purpose any species might be taken, but the one selected to illustrate growth in animals is the frog, not only because it is familiar to every one, but also because it lends itself conveniently to observation and has been thoroughly studied.

The life-history of the frog begins with the fertilized ovum, and accordingly this will be the starting-point. To give an idea of the amount of growth which will take place it may be mentioned that the ovum of the frog is about 2 mm. in diameter, while the adult may be over 15 cm. long, so that the increase in size is considerable. Even this, however, is not one of the most striking cases, for the mass of the human adult is fifteen billion times that of the human ovum.

Development is started by fertilization, which consists in the fusion of a male reproductive cell or spermatozoon with a female ovum; and as a result of this stimulus the ovum begins to divide. Like all cells the fertilized ovum contains a nucleus, which divides at the same time as the cell, so that all the cells produced by division from any cell each contain a nucleus. The process of cell division is characteristic throughout animals and plants, and the chief thing to remember about it is that the nucleus of a dividing cell is accurately halved between the two daughter cells to which it gives rise.

The fertilized ovum splits into two equal parts, and each

of these divides again. This process is continued until the whole of the ovum is divided up into a large number of small cells which remain together in a cluster and rather resemble a blackberry [Morula stage]. Now the original ovum contained yolk, which, being heavy, sank to the lower pole of the ovum. [It is impossible to speak of the " bottom " of a sphere.] Consequently, after division of the ovum, those cells which are situated at the lower pole are filled with yolk and are light in colour. The cells at the upper pole contain no yolk, are darker and also are smaller and divide faster than the yolk-containing ones, for the presence of masses of the heavy inert substance in the latter delays their division.

As a result of division, where there was one cell, the ovum, there is now a large number. The total amount of protoplasm, however, is no greater and there has been no increase in size. The increase in the number of the cells has been accompanied by a corresponding decrease in the size of the cells themselves. There has therefore been no growth. But the amount of substance contained in the nuclei of all the cells derived from the ovum together is much greater than that which the nucleus of the ovum originally contained. This means that new nuclear substance has been produced from the protoplasm of the cells during this division.

As division proceeds a cavity appears in the middle of the " blackberry," in the midst of the cells. This cavity fills with fluid and as a result of the displacement so caused there is a slight increase in size of the whole organism which is now a hollow ball with thick walls [Blastula stage].

Up to this stage, cell division has been almost the only process which the organism has undergone. The small increase in size which has occurred is due to the absorption of water into an internal cavity, and differentiation of shape has been limited to the production of smaller dark cells at one pole, larger light yolk-containing cells at the other, and a central cavity.

The next events in development entail growth and differentiation as well as cell division. At this stage the organism is a hollow ball with a single wall. Now all animals above the very lowest are really double sacs, one inside the other. The outer sac is the external skin and the inner one is the alimentary canal within which the food is digested. The next step in development is therefore concerned with producing a double-walled sac out of a single-walled ball. This is brought about by the growth of cells of the upper pole outside and over those of the lower pole so that two layers are formed, one inside the other.

The dark cells touch the light ones along a ring which runs round the ball like an equator. At one point on this ring the dark cells project and begin to overlap the light ones, forming a small projecting lip. Seen from the lower pole at this stage the organism presents a white hemisphere with a ring of dark cells just appearing round the equator. The lip extends downwards and the dark cells grow over the light ones so that the white hemisphere underneath begins to get reduced. At the same time the lip of overgrowth which started at one point extends round the equator both ways, meeting on the other side. The dark cells then grow down as a cylindrical curtain enveloping the light cells. As the curtain descends the white area seen from beneath gets smaller and smaller until it reaches a definite and small size.

What happens during this process is readily grasped when seen in sections, in which the formation of the lip of overgrowth and its extension downwards over the underlying cells are plain. The result of this overgrowth of one kind of cells by the other is the formation of two layers, an inner and an outer. Between the two layers are the remnants of the cavity which occupied the centre when the organism was a simple hollow ball. It is squashed nearly out of existence and almost obliterated as the two layers lie closer together. Instead there is a new cavity which is enclosed by the inner layer and opens to the exterior through the hole left open when the dark cells ceased growing over the others. This

cavity is the primitive gut, out of which the digestive system is formed, and the hole through which it opens to the exterior is called the *blastopore.* The ring just round the blastopore is where the inner and outer layers meet, and is of great importance in the further growth of the animal [Gastrula stage].

This growth and separation of two layers one within the other is a very important step in moulding of shape [morpho-

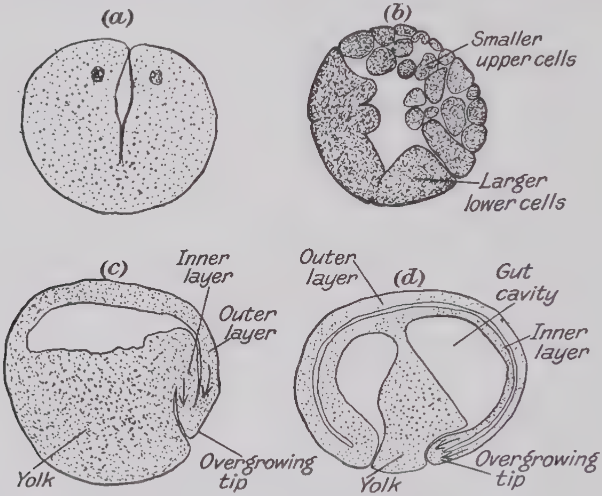

FIG. 3.—The early growth of the frog. (*a*) The ovum has split into two cells. (*b*) "Blackberry" stage with many cells, the upper ones smaller than the lower. (*c*) Beginning of the formation of the overgrowing lip. (*d*) The lip has completely overgrown the lower hemisphere, with the exception of a small hole through which the yolk protrudes.

logical differentiation], for it separates from each other the elements from which the various tissues and organs of the adult will be formed. The outer layer or *ectoderm* will give rise to the external skin, hair, feathers and scales (the latter three do not occur in the frog), organs of sense such as the nose, the ear, the eye, and to the brain and nerves. In fact, it is concerned with everything dealing with the outside of organism ; skin to enclose it, ears to hear, noses to smell the outside world, eyes to see, and of course one of the chief functions of the nervous system is to inform the organism of what is going on outside it.

The inner layer consists of the cells which contain yolk. This layer undergoes a further splitting into two, resulting in a layer surrounding the gut cavity, the innermost layer or *endoderm*, and another between the latter and the outer layer, which, since it is in the middle between them, is called *mesoderm*. From the innermost layer or endoderm there arises the lining of the alimentary canal and of all its derivatives. These are the lungs, liver, thyroid gland, pancreas or sweetbread, bladder, and a primitive supporting rod which extends along the dorsal side of the gut beneath the spine, the *notochord*. This rod is later replaced by the vertebral column.

From the mesoderm or middle layer the remaining tissues and organs are formed, to wit: muscle, cartilage, bone, so-called connective tissue which acts as padding between the other tissues, and the reproductive organs.

These three layers, ectoderm, endoderm and mesoderm, can be recognized throughout the animal kingdom above a low grade of evolution. They always give rise in development to the same class of tissue, and the process of their separation is very important.

The organism can now be definitely orientated, and its various regions may be referred to axes and compared with the adult. The blastopore, which is the opening into the primitive gut, arose at the lower pole of the embryo. As a result of the rotation of the whole embryo owing to the displacement of the heavy yolk, the blastopore comes to lie at the side, and in this position it marks the posterior end of the embryo. At the opposite pole (which was the upper pole of the ovum) is the anterior end where the head will develop. The point at which the lip of overgrowth (forming the blastopore) first appeared is dorsal and marks the middle line of the back, and opposite to it of course is the ventral surface.

The organism is still spherical. Nearly all animals are longer from head to tail than they are broad from side to side, and this lengthening of the head-tail axis is the next stage in development. In order to see how this is brought about it must be remembered that just round the rim of the

blastopore the endoderm and ectoderm are in contact, and as a matter of fact the mesoderm is too. Consequently, if growth were to take place round the blastopore, all three germ layers would be involved in it, and growth in only one region (the rim of the blastopore) can contribute to all three layers. This is, in fact, what actually happens, for the rim of the blastopore is composed of rapidly-dividing cells, and is a zone of active growth. The cells divide along the head-tail axis of the organism, and the blastopore gets further and further away from the anterior extremity, by intercalating new cells just in front of itself. In this manner the organism

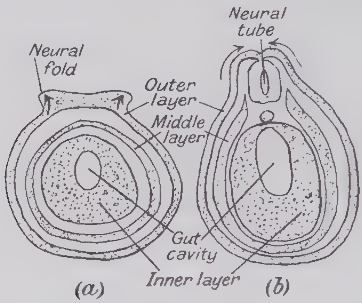

FIG. 5.—The growth and formation of the spinal cord. In (*a*) the two neural folds are shown which grow up in the direction indicated by the arrows. In (*b*) these folds have met, enclosing a tube beneath them, which is the spinal cord.

grows in length and loses its spherical shape. As it moves backwards the blastopore contributes new cells to each of the three layers, and so they all keep pace with each other.

During this period the organism is increasing in size by absorption of water, enlargement of the contained cavities and elaboration of the yolk into new protoplasm from which new cells are formed.

Along the dorsal surface two folds of ectoderm grow up, extending from the anterior to the posterior end and thus forming a groove between them. These two ridges eventually fuse together over the groove and in this manner convert it into a tube. The tube becomes the spinal nerve-cord and its expanded front end is the brain. The brain and spinal cord are hollow and the cavity they contain is that

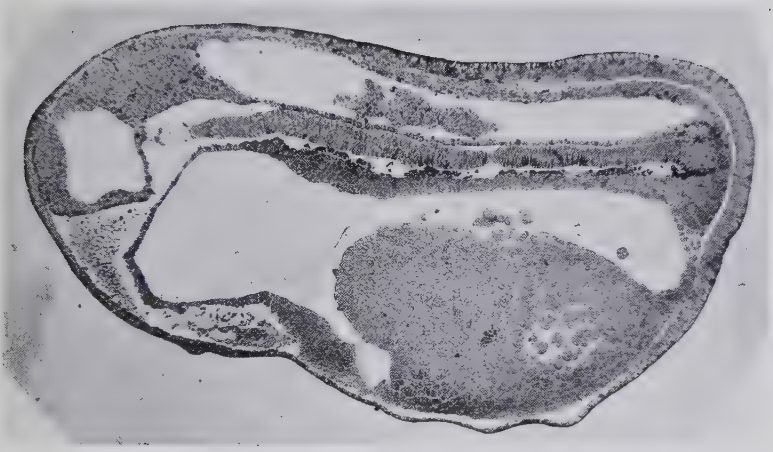

FIG. 4 (*a*).—Photograph of a longitudinal section through a young embryo of a frog, which has by the activity of its cells round the blastopore departed from the spherical condition and grown in length. The mouth has not yet broken through to the gut.

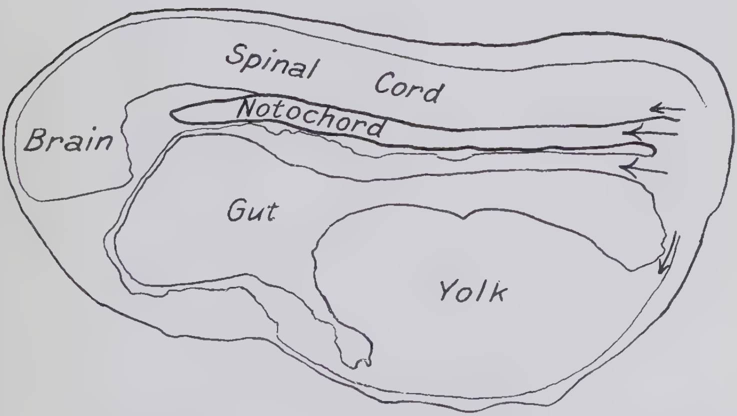

FIG. 4 (*b*).—Interpretation of Fig. 4 (*a*). The arrows show the direction in which new tissue is added to all the layers, so that the region of the blastopore continually moves backwards.

which was enclosed by the two ridges when they met over the groove between them. The main nervous system is therefore moulded (morphologically differentiated) by growth in particular places resulting in the formation of the ridges [Neurula stage].

Underlying the spinal cord along most of its length is the primitive skeletal rod, the notochord, which gives rigidity to the embryo and which has arisen by separation from the roof of the gut cavity.

Thus far growth has not only produced an increase in size of the whole organism, but by growing at particular places and in certain directions more rapidly than in others the organism has acquired a well-defined shape and the rudiments of future organs have been roughly blocked out. The mass of clay is beginning to resemble the finished sculpture which it is aiming to copy. Growth has produced morphological differentiation. The mouth and gill-slits break through the walls of the embryo and place the gut cavity in communication with the exterior, the gut cavity becomes the alimentary canal and the tail grows longer as a posterior prolongation of the dorsal portion of the embryo.

When the embryo is hatched as a tadpole its store of yolk is nearly exhausted, and it leads a free and independent life. It feeds vigorously and its size increases very rapidly, especially the length of the tail, which is used for swimming.

It is time now to talk of what the cells themselves have been doing. At the start the only difference between any of them was that some contained yolk and others did not. They were just simple corpuscles of protoplasm more or less spherical in shape and devoid of any peculiar structure whatever. It is important to have a word to denote this condition, and accordingly such cells are called *embryonic* since they are characteristic of embryos. But as development proceeds and various organs and regions are marked out, the cells of these regions assume particular shapes and structures adapted to the functions which they will have to subserve. In this way tissues are formed, and tissues compose

organs the characteristic of which is to do a particular kind of work, and in order to do that work its constituents must possess the necessary structure. Thus the cells composing the skin and lining cavities are moulded to form an epithelium, a tissue which spreads over and covers the underlying structures. The cells of the nervous system assume the characteristic form of nerve cells. Muscle is composed of cells containing contractile fibres which enable the muscle to contract and expand. Other cells embed themselves in a stiff gristly substance of their own making and thus form cartilage. Yet other kinds of cells form bone, glands, blood and the remaining kinds of tissue. These changes which the cells undergo are called histological differentiation. A differentiated cell is in the opposite condition to one which is embryonic, for instead of consisting simply of pure protoplasm it contains various structures such as fibres, etc., the presence of which actually makes it differentiated.

This differentiation of cells and tissues is not growth from the point of view of the whole organism, since its size is not thereby increased. When considering a particular tissue, however, it may be said to grow as differentiation proceeds. Thus a bone, for instance, increases in size as more and more cells turn to producing it. On the other hand, histological differentiation is one of the most important causes preventing growth of the whole organism, for when a cell is differentiated it contains or is surrounded by an accumulation of structures which are inert and more or less rigid and which impede the process of cell division.

Histological differentiation, therefore, sets in rather late in embryonic life and proceeds to the perfection of the regions and organs which have been roughed out by morphological differentiation and growth.

After an active life for a certain time as an aquatic animal, breathing by gills and swimming by means of a tail, the tadpole begins to show changes which will convert it into a frog. The adult frog is a land animal, breathing by lungs, moving about with the help of four limbs ending in fingers. The

changes which bring about this result are known as *metamorphosis*. There have been many tales of metamorphosis in history and in legend. In Greek mythology Zeus was sufficiently fortunate to be able to metamorphose himself (and other people too) at will into any animal which best suited his immediate needs. Science knows nothing of these exploits, but the metamorphosis of the tadpole into the frog, if less sensational, is none the less interesting, and has the advantage of being a true occurrence and open for anyone to observe.

There is a rapid change of structure and function in adaptation to a changed mode of life. It entails growth of the limb rudiments, of the lungs as organs of breathing to take the place of the gills, which shrivel up. The gill-slits close up and disappear. There is increase in size of the tongue, stomach, liver and eyes, but decrease in the intestine, and most markedly in the tail, which is completely absorbed and disappears. During metamorphosis the animal does not feed, and there is a decrease in the mass of the body as a whole.

Thus the final stages of development in the frog entail growth of some parts and "degrowth" or reduction in others. This differential growth of parts is of common occurrence among animals and there will be reason to refer to it again.

After metamorphosis the frog feeds again and soon grows up to its full adult size. It has now been traced from the ovum, and it has been shown how cell-division, growth, morphological and histological differentiation have been at work upon it to produce the finished article. One of the most important things to deduce from this survey is the fact that growth takes place from cells which are undifferentiated and embryonic. Why this is important will soon be apparent.

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CHAPTER III

GROWTH IN PLANTS

The life-cycle of the frog was taken as starting from the fertilized ovum, which is the earliest stage at which a definite individuality can be assigned to the future organism. The life-cycle of a plant, such as a wallflower, also starts from the fertilized ovum, but the question is, where is it in the plant and what does it look like ? Most people imagine that the seed is the starting-point of the new individual, but this is wrong, for, as will be seen later, the seed is already a well-formed embryo besides many other things as well. In animals the ovum is easy to recognize as a cell freed from the ovary, but this is not the case in plants.

The reproductive organs are, of course, to be found in the flower. In the pistil a number of oval-shaped bodies are formed known as ovules. These are fairly large and consist of hundreds of cells. Inside the ovule there is to be found a cell which is the ovum. The anthers produce pollen grains, which when ripe contain the representatives of three cells, one of which is the spermatozoon.

The pollen is liberated, and as it is very light, it is carried about in the air and a certain number of grains will fall on to the stigma or pillar which surmounts the pistil. This constitutes *pollination*, which must be distinguished from *fertilization*. The latter is the union of two reproductive cells, and this has not yet occurred.

On the stigma the pollen grain absorbs the sticky juice containing sugar which is produced there, and it then swells and grows so that the contents of the grain push through

its shell and protrude in the form of a tube. This tube gets longer and longer and sinks into the pistil until it reaches an ovule. This it enters, and it then finds the ovum. As soon as that has happened the nucleus in the pollen tube, which represents the spermatozoon, fuses with the ovum and fertilization is effected.

The ovum divides and produces a string of cells. One end of this chain is fixed to the wall of the cavity in the ovule which contains it and in which the embryo develops, the other hangs free within it. It is the cells of the latter end which will produce the embryo, which, by increasing in size and in number of cells, grows into a structure which

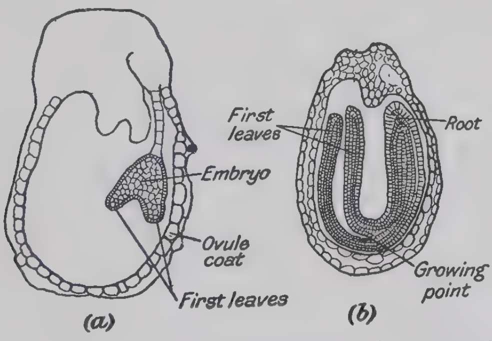


FIG. 6.—(*a*) A very young embryo of Capsella in the ovule. (*b*) An older and more developed embryo in the seed.

is more or less heart-shaped. The two projections will be the two first leaves of the seedling, and in the niche between them the stem of the plant will grow out. Near the opposite end, the point of the heart, the root will be formed.

The embryo continues to grow, deriving nourishment from the mother plant; but after a time its development ceases and it lies dormant and awaits the stimulus to further growth. While all these things are happening to the embryo other events are taking place of great importance; the ovule is being converted into a seed and the flower is being turned into the fruit. These two events are interesting inasmuch as they are examples of growth which are not part of the embryo, but result in the forma-

tion of structures which are accessory to it and help it in its later development.

The skin of the ovule becomes the coat of the seed, which is hard and resistant. The growth of the fruit, which means its ripening, may affect only the pistil in some flowers, in others it may involve the whole flower or indeed groups of flowers close together on a stalk, as in the pineapple. It may also be brought about by many different ways. A familiar example is the apple, which is formed from the small flower of apple blossom. The skin and fleshy parts of the apple are formed from the basal part of the flower which is underneath the sepals and petals, enormously expanded by growth and cell division. In the centre are the pips or seeds, which were the ovules, and inside each of which there is an embryo.

The function of the flower is to produce seeds, protect them, and to liberate them at the right time. Eventually the seed finds itself on the ground where it waits for the weather to be sufficiently warm and moist. From this point the development of the embryo may be resumed.

The presence of water and a suitable temperature stimulate the embryo to renew its activities of growth after a quiescent period which may have been of considerable length. The root elongates rapidly and projects through the hole in the seed coat into the ground, and the first two leaves unfold into the air. This sprouting or germination is done at the expense of food materials such as starch and fat stored up in the seed and originally derived from the mother plant. After germination the seedling nourishes itself in the manner characteristic of all green plants; water is absorbed by the root together with the salts in solution in the soil, carbon dioxide is captured from the air by the leaves, and by means of this modest menu the seedling continues to grow.

The later history of the plant is concerned chiefly with the growing points, that of the stem and that of the root. Once the seedling has been formed in the manner described

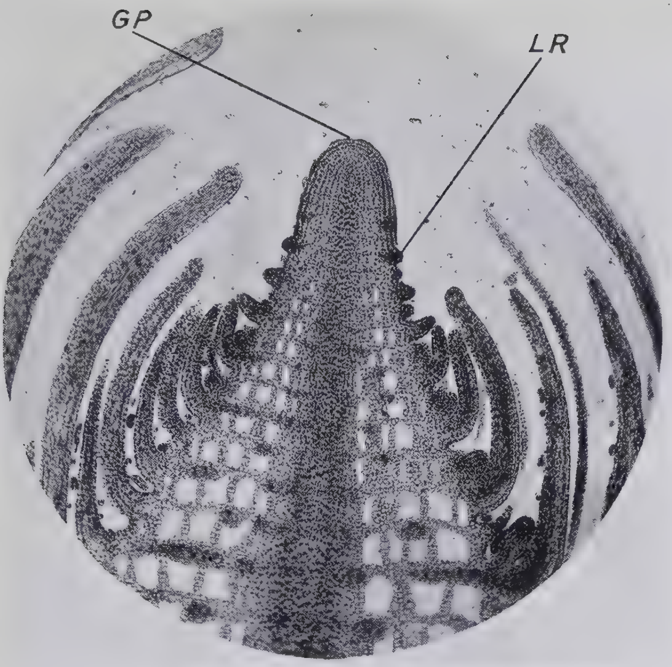


FIG. 7.—The growing point of a stem of Hippuris in longitudinal section. The growing point (*GP*) is domed and composed of many small cells. At the sides the leaf rudiments (*LR*) appear, getting larger the further they are from the growing point.

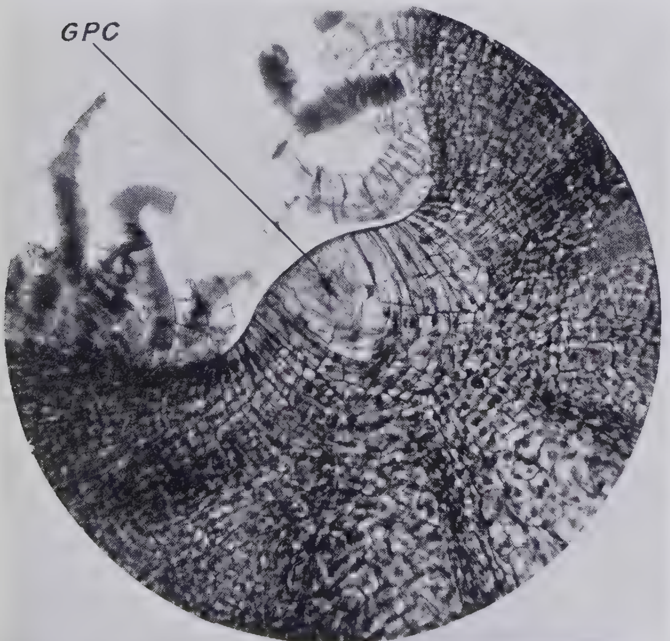


FIG. 8.—The growing point of the stem of a fern, which is composed of a single large cell (*GPC*).

above, the rest of the plant is largely the result of the activities of these growing points.

These growing points are one of the most important features of plants as compared with animals. They do not differentiate but remain growing points, and their cells are always embryonic. They are, as it were, permanent embryos, always growing and adding to the structure of the plant as long as it lives.

The growing point of a stem of the wallflower consists of a mass of small actively dividing cells, rich in protoplasm and devoid of any differentiation. Such a region is often spoken of in plants as being *meristematic*, which means much the same thing as embryonic. In the ferns there is one large apical cell which divides continuously. The apical surface is slightly dome-shaped, and just at the side of the dome small swellings are seen, which are larger the further they are from the apex. They are just accumulations of cells and represent the rudiments of the leaves.

The production of the little leaf rudiments is due to growth taking place faster at these particular spots than at others, and the result, with its moulding of shape, is of course what has already become familiar in the frog as morphological differentiation. There will be some more to say about this in plants in connexion with the arrangement of the leaves on the stem. Turning to histological differentiation, however, and to the specialization of the cells themselves, in plants it is brought about in a characteristic manner, differing from that which obtains in animals. As the growing point travels upwards, it leaves behind and beneath it the cells to which it has just given rise, much as the active zone of growth round the blastopore moves backwards, leaving the newly-formed cells. In the plant these cells, which have just been produced by the growing point, absorb water and undergo swelling. This swelling mostly occurs in one direction and produces a great elongation of the cells, and the result of this increase in size of the individual cells in the zone just beneath the growing

point is naturally to raise the growing point itself higher and higher into the air. In this manner the stem gets longer, and its growth is due first to the production of new cells and then (and this is the more important of the two) to the increase in size of the individual cells due to the absorption of water. The enlargement of the cells has been almost entirely produced by the distension of water without any increase in the amount of protoplasm of the cell. The action of water in producing a state of stiffness in plants is familiar, for it is well known how they droop and fade when too dry.

At the same time the stem grows to a certain extent in thickness, and since there is another method by which stems thicken, this is called primary growth in thickness.

After the phase of elongation further differentiation of the cells sets in. They, of course, no longer divide, and proceed to specialize their walls rather than their contents. The cell wall, which is at first a simple membrane covering over the surface of the protoplasm of the cell, becomes converted into a thick partition made of some hard substance, in some cases of wood. Certain cells communicate end to end and form conducting vessels grouped together into bundles which are accordingly called *vascular bundles*. Through them transport up and down the stem is effected. The rigidity of the materials of which the walls of the cells are composed makes it possible for these to function as a skeleton and support the stem, maintaining an erect position.

The growing point of the root is very like that of the stem. It constantly sinks downwards into the soil and produces new cells so that the root lengthens. The growing point is a delicate structure and would soon be damaged if it had to bore through the soil as a nail is driven into wood. To prevent this, there is a small protective covering known as the root cap. This is constantly worn away and replaced. The growing point of the root is therefore not quite at the tip.

The function of a root is to provide a firm anchoring and

pedestal for the plant to absorb nutriment from the soil and to excrete certain substances. For these purposes roots extend and branch so as to cover as large an area as is necessary. Branches in roots arise by growth from cells which are deep-seated. As a result of growth and cell division the young root branch passes through the outer layers of the parent root and emerges protected by a little root cap.

Leaves arise, as has been mentioned from little accumulations of cells just at the side of the apex of the growing point. They undergo elongation, and differentiate into the fully-formed leaf.

The arrangement of leaves on the stem is not a haphazard one. In some plants a whole group of leaves may occur at the same level of the stem, radiating from it like the spokes of an umbrella. In such cases they are symmetrically arranged, and the angles between any two adjacent leaves are equal. That is to say, that if there are two they will be opposite each other, four will be arranged in the form of a cross, and so on. Such a group of leaves at one point is a whorl, and the leaves of one whorl usually correspond with the gaps between the leaves of the next whorl, so that they alternate.

In a large number of cases, however, the leaves are not symmetrically placed, only one comes off from the stem at any level, the next leaf being at a different height, and also a certain distance away round the circumference of the stem. Such a plant gives the appearance of its leaves being arranged in a spiral (strictly a helix) winding round the stem, and one can imagine oneself climbing up the stem by treading on the successive leaves as steps of a spiral staircase. It was the custom to denote the particular kind of leaf arrangement by counting the number of turns taken by the spiral round the stem between any leaves situated the one exactly over the other, and the number of leaves passed in these turns of the spiral. The leaf arrangement of the wallflower, for example, is usually taken as $\frac{2}{5}$,

meaning that there are two turns of the spiral and five leaves between any leaf and the one exactly above it.

The trouble is, however, to determine whether a leaf is exactly and accurately above another. More careful observation has shown that in these plants with asymmetrical leaf arrangement, no two leaves are ever situated in the same vertical plane, although they may be close to it. In the stonecrop, an illustration of which is reproduced in Fig. 10, two turns of the spiral pass five leaves, but the sixth is not immediately below the first (counting the first as one), so that the arrangement is not $\frac{2}{5}$. Three turns of the spiral bring one to the ninth leaf, but that again is not under the first; it is therefore not $\frac{3}{8}$. Five turns and the fourteenth leaf $\left(\frac{5}{13}\right)$, eight turns and the twenty-second $\left(\frac{8}{21}\right)$, or thirteen turns and the thirty-fifth $\left(\frac{13}{34}\right)$ leaf are progressively better approximations to a leaf immediately beneath the first, but they are not exact.

As a matter of fact, in these arrangements no two leaves are ever exactly in the same line. In the fractions which have just been given and which represent the ratio between the number of turns of the spiral and the number of leaves, it is worth noticing that the figures of any fraction are the sum of the figures of the two fractions immediately before it. Thus $\frac{2}{5} + \frac{3}{8} = \frac{5}{13}$, $\frac{5}{13} + \frac{8}{21} = \frac{13}{34}$. This succession of figures, in which the next one is always obtained by adding on the last, is known as the *Fibonacci Series*, and it has many curious mathematical properties. One of these is that in plants with such a leaf arrangement, each leaf tends to make an angle of $137\frac{1}{2}$ degrees with the preceding one. The result of this is that a leaf is always formed in the largest remaining gap, and far from resulting in superposition, this arrangement ensures that theoretically no two leaves will ever be superposed. In practice this works out

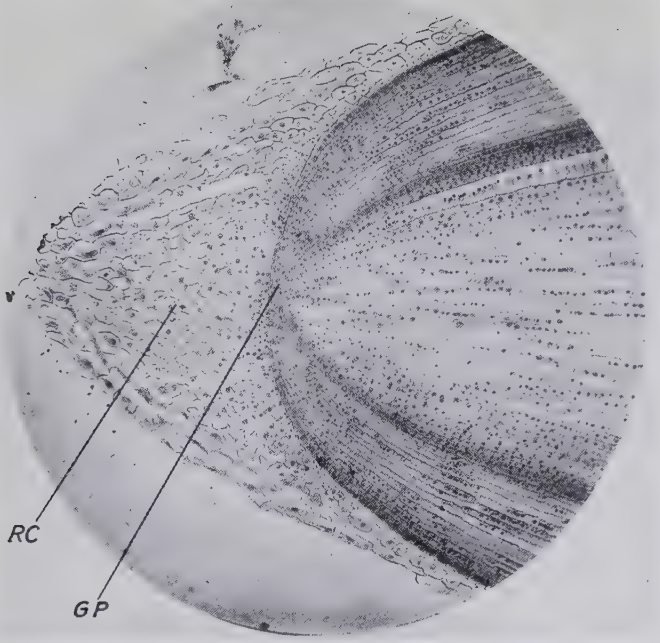
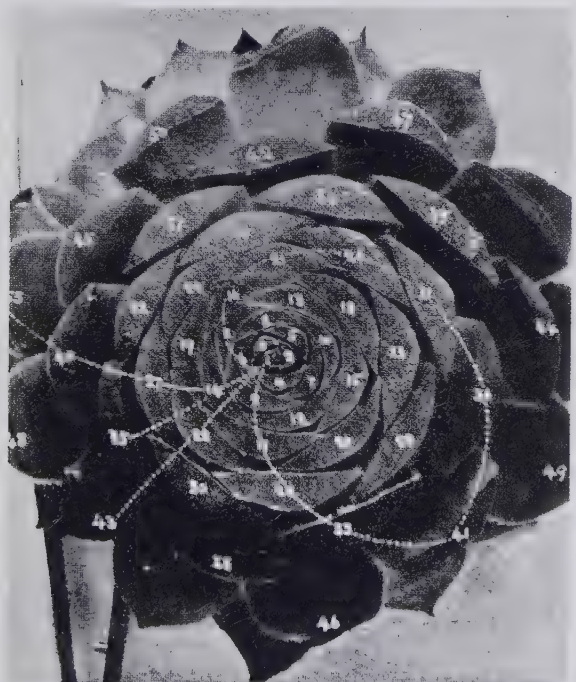


FIG. 9.—The growing point of the root of the maize plant, showing the actual growing point (GP) and the protecting root-cap (RC).



[From Church.

FIG. 10.—The arrangement of the leaves in the stonecrop. The numbers refer to the position of the leaf in the spiral, starting from the centre. No two leaves are really in the same straight line from the centre.

at the result that superposition is reduced to a minimum, and the advantage of this is obvious when it is considered that the functions which leaves perform require them to receive as much light as possible.

Now, the arrangement of the leaves is determined just at the side of the growing point by unequal rates of growth

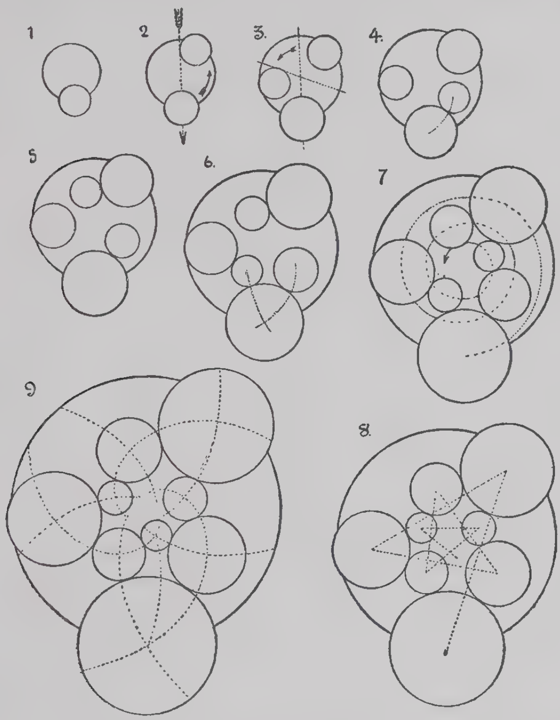


FIG. 11.—The order of development of leaf rudiments near the growing point, showing that the next leaf arises in the largest remaining gap. (From Church.)

in different directions; in other words, it is morphological differentiation, and the reason why it has been discussed here at such length is interesting. A tree bears branches, and if the tree be high and the branches heavy, it will not be able to stand up straight unless the branches are evenly balanced round it. Now, a branch only grows out in the angle between a leaf and the stem, so that the arrangement

of leaves also determines the position of the branches. When a single leaf (and branch) is produced at a time, the only way for the balance of the tree to be maintained is for each leaf to form at a constant angle from the preceding one. This is effectively what happens, the angle being $137\frac{1}{2}$ degrees. The tiny accumulations of cells round the growing point are, therefore, responsible for the tree being able eventually to maintain itself erect.

A stem which grows in length must also grow in thickness if it is to withstand successfully the mechanical strains to which it will be subjected. It has already been mentioned that a certain amount of primary growth in thickness occurs, but not very much. Some other way of growing in thickness is required or the stem cannot grow very high. No such method exists in that group of plants of which the lily is an example, and consequently they do not grow to any great height. In others, such as elms, oaks, and conifers, a zone of cells which are meristematic and embryonic appears, called the *cambium.* In these forms the stem contains a number of vascular bundles arranged in the form of a ring. Each bundle is made up of wood on the inside towards the centre, and bast on the outside. Between the wood and the bast is a layer of cells, not highly differentiated, and capable of cell division and growth, the cambium. When secondary growth in thickness is about to take place, the cambium layers of neighbouring bundles become united by a layer of cells which have become embryonic, and the cambium thus forms a complete ring. By cell division and growth it produces new wood on the inside and new bast on the outside, so that the stem itself increases greatly in thickness.

Owing to climatic conditions growth in non-tropical regions takes place at different rates according to the time of the year. This is reflected in the annual growth rings which appear in a section of a stem, and by counting which the age of the plant may be ascertained. The absence of these growth rings in fossil plants is taken to mean that the climate at the time when the fossil lived was tropical.

Secondary growth in thickness of the root takes place in the same way as in the stem, by an active cambium ring.

Plants like the lily have no cambium, and yet a very few of them manage to reach a considerable height, but in all these cases some other mechanism is at work to thicken the stems. In palm trees the increase in thickness is due to greater swelling of the existing cells. In the Aloe, Yucca and Dracæna, a ring of embryonic tissue arises outside the vascular bundles (and therefore not the same thing as the cambium) and increases the thickness of the stem.

A bud is a growth out from the stem in the angle between the latter and a leaf. Some buds possess growing points and produce branches which increase in length; others give rise to flowers. Flowers consist of modified leaves, in different whorls. The lowest are the sepals, then come the petals, and next the anthers, which are so much modified that they do not resemble leaves at all. The sepals are usually green, like the foliage leaves, the petals are usually coloured but are easily recognizable from their shape as leaves. At the apex of the axis which bears these leaves the growing point disappears and a set of leaves arise, the carpels, which form the pistil containing the ovules. In the ovule is the ovum from which this description of the life-history started.

On comparing the processes of growth in plants with those in animals there are many differences, but there is one great similarity which is worth stressing and repeating here: viz., the regions which grow are undifferentiated and embryonic, and little or no growth takes place from differentiated tissues.

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CHAPTER IV

OTHER INSTANCES OF GROWTH IN ANIMALS

The frog grows in length by the activity of the cells round the rim of the blastopore. In such animals as the earthworm great elongation takes place by means of a zone of growth at the posterior end of the animal. This zone continually produces new cells on the anterior side, so that the posterior end of the animal gets further and further away from the head. In these cases the animal is split up into a number of regular equal-sized blocks along its length, each of which is a segment. The earthworm and its allies grow in length by a continuous repetition of a definite pattern, and new segments are added on to the hind end of the animal, just in front of its tail, which thus gets pushed further and further back. In some species the cells divide to produce as many cells as there will be segments, each segment developing from the proliferation of one of these cells. The existence of a zone of growth at the posterior end of the body is of general occurrence in worms. In the tapeworm, however, the "head," which remains attached to the wall of the alimentary canal of its host, continually produces new cells, which pass back as yet newer cells are intercalated between them and the head. In this manner the "tape" is produced, which may reach a con-

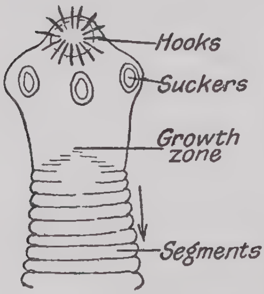

FIG. 12.—The head of a tapeworm, showing the growth zone where new segments are produced. Segments continually pass backwards as they grow older in the direction indicated by the arrow.

siderable length. In this case the zone of growth is different from that at the posterior end of other worms, and has been independently evolved.

Hair does not occur in the frog, so that it was not included in the description of that animal, but it may conveniently be dealt with here. From the living layer of the skin (which just underlies the outer horny layer) an inpushing takes place which becomes the little pit or *follicle* in which the hair develops. A hair is simply composed of modified cells, horny in nature, arranged in the form of a cylinder.

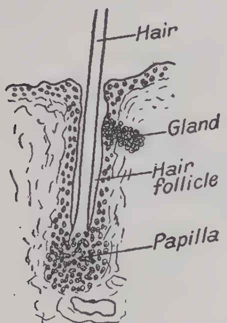

FIG. 13.—A young hair in its follicle. At its base is the papilla, where new cells are added on to the hair from beneath, and thus push it upwards.

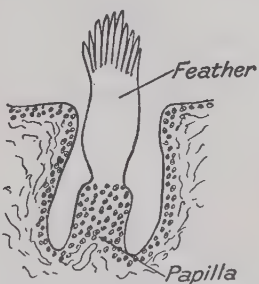

FIG. 14.—A young feather growing from its papilla. It is fraying at the tip to form the barbs.

The hair is attached to the bottom of the follicle, at which place the cells, which are rich in protoplasm and well supplied with blood, divide and produce more cells, which are added to the hair from underneath. In this manner the tip of the hair protrudes from the follicle and the hair grows longer.

Feathers grow in a somewhat similar way, except that they start as an outpushing or papilla, which later becomes sunk in a sac. The outer end of the feather frays out and produces the barbs and barbules, while by growth at the base the length of the feather increases.

In the case of teeth, a layer of skin sinks into the gums and its cells produce a thimble-shaped cap of enamel. Inside this cap the tooth papilla produces a hard substance not

unlike bone, known as *dentine*, of which the body of the tooth is composed. The tooth grows as more dentine is added and at a certain time it erupts through the gum and projects into the mouth.

While it does not contribute to the growth of the organism, differentiation of tissues may produce increase in size of particular organs and structures. Bones enlarge as their differentiation proceeds, but in this case the growth is peculiar in that addition of new bone in one place is often accompanied by its removal in another, so that there is a regulation of shape during the increase in size. In the case of the thigh bone, for example, at the same time as

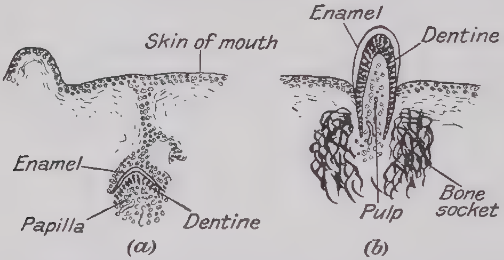

FIG. 15.—(*a*) The rudiment of a tooth below the gums. An ingrowth of skin produces the cap of enamel, beneath which dentine is formed. At the base is the papilla supplying blood. (*b*) The tooth after eruption and covered by its enamel cap. The interior is occupied by the pulp, and round the base bone has grown so as to hold the tooth firm in a socket.

new bone is added to the outside it is removed from the inside, so that the marrow cavity increases with the growth of the bone. This is beautifully shown by experiments on feeding with madder. The new bone made during this diet is of a particular colour, and can be recognized as a ring round the outside when the bone is seen in section. If the diet is stopped and the bone is examined later, it is found that the dark ring is no longer on the outside, as normal bone has been formed outside it. Later still the dark ring will be on the inner side lining the marrow cavity, and eventually it will disappear, showing that as bone is added to the outside it is removed from the inside.

The actual process of formation of bone consists in the deposition of calcium salts by particular cells. At first they give rise to irregular spicules, and then the continuous addi-

tion of calcareous matter joins these together to form the porous structure familiar as bone. Since it is formed outside the cells which give rise to it, bone is an intercellular substance.

In molluscs, such as snails or mussels, the outer surface of the body produces a shell of lime lined with mother-of-pearl. This shell increases in size with the animal, and in many cases its shape remains the same although its size increases. This involves a pretty little geometrical problem, which the animal solves in the following way. There is in geometry a class of figures called *gnomons* whose peculiarity it is that when they are added to another figure, the resultant figure is similar in shape to the original, though of course larger in size. Now the successive additions to the shells are gnomons, so that their shape is not altered while they grow.

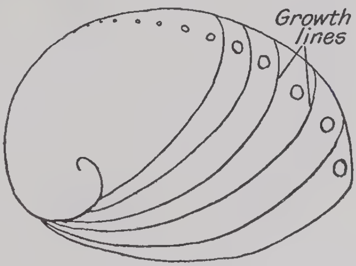

FIG. 16.—The outline of an Orm Shell with some of the growth lines indicated. Each successive addition leaves the shell of a similar shape, and is a "gnomon."

One of the most striking features of the Southern Seas is the presence of large reefs formed by corals. These masses of calcareous matter are of sufficient importance as to be classed among the various kinds of rocks of which the earth's surface is composed. They are the product of the coral animals, which are like sea-anemones and which produce this calcareous skeleton round themselves as a protection and support. By the growth and increase in number of the animals and the accumulation of their skeletons reefs are formed.

Bones, shells and coral are all examples of the growth of inorganic substances outside cells. The growth of ova in the ovary before they are laid is an example of the increase in size of single cells. All the food supply of the young embryo, until it is sufficiently well developed to feed itself, is derived from the nutriment contained in the ovum in the form of yolk (except in mammals, where a special connexion

exists between mother and young for the nourishment of the latter). As the yolk accumulates in the cell the latter increases in size until, in the case of the fowl for instance, it reaches relatively huge dimensions.

Another case of growth of cells may be seen in nerve cells. Nerves are the paths along which stimuli are transmitted, either from a sense organ to the brain, or from the latter to a muscle, and they consist of long thin outgrowths of the nerve cells. During development nerves grow out from the nervous system to their various destinations, which may be quite a long way away. In some nerves the whole distance from the sense organ to the spinal cord is spanned by long extended processes of single cells. In the elephant, for example, the nerve from a touch-spot on its hind foot to its spine is of a considerable length for a process of a single cell.

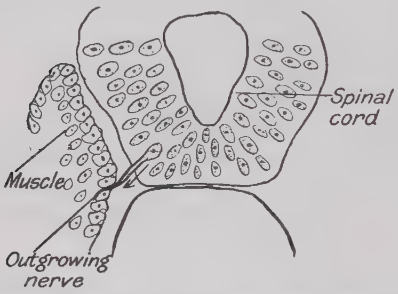

FIG. 17.—Diagram of a transverse section through a very young dog-fish showing a nerve cell growing out to a muscle and forming a nerve.

If one were suddenly asked "What are the things which grow?" the answer would be, "Young individuals, of animals and plants," and in the main this is correct. There do, however, exist cases of growth which are peculiar in that they do not result in the production of a new individual. Already some examples of this have been seen in plants, where the ovule and the flower both grow, the one into the seed, the other into the fruit, but neither of these structures is a new individual. A similar sort of thing turns up in animals among the higher vertebrates. There, complications occur as a result of which the whole of the ovum does not become a new individual, but part of it develops into various organs and membranes which carry out certain functions for the embryo until it is hatched or born; they do not form part of it.

In reptiles, birds, and mammals, the skin at the side of the embryo grows up and over it, eventually completely covering and enclosing it within a cavity. The membrane of this cavity (the *amnion*) will never be part of the embryo, but is developed to protect it; for, being filled with fluid, it acts as a water cushion and deadens any shocks which may shake the egg shell. All the ancestors of these animals underwent their early development in water; reptiles, birds and mammals reproduce on land, but by means of this

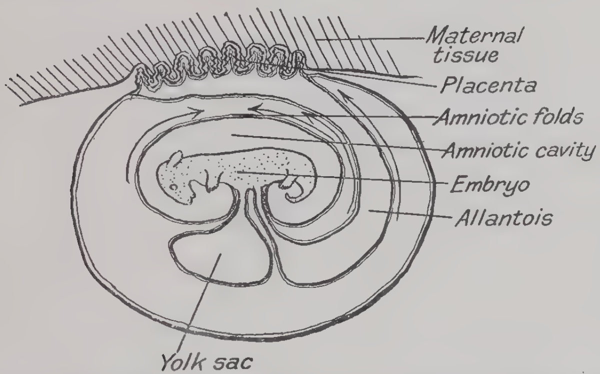

FIG. 18.—The embryonic membranes and placenta of a mammalian embryo. The embryo itself is dotted. The amniotic folds have grown over it (in the directions shown by the arrows), and the allantois has grown out to the placenta.

liquid-containing cavity their young embryos are able to develop in a fluid medium. It may therefore be said to represent the " primitive pond " in which their ancestors developed.

Towards the hind end of the alimentary canal there grows out a sac, which, in the frog, gives rise to the bladder. In higher forms it grows also into a large bag (the *allantois*), which in birds and reptiles applies itself to the inside of the egg shell. The shell, which is porous, allows air to pass through it and this permits an interchange of oxygen and carbonic acid gas to take place between the blood-vessels of the bag and the atmosphere. In fact, this bag functions as a respiratory organ and without it the embryo could not breathe.

In the mammals the allantois assumes very great importance since it enters into the formation of the organ whereby the embryo is nourished by the mother (the *placenta*).

Through this the embryo derives practically all its food and oxygen and also gets rid of its waste products. The placenta is an organ which brings the bloods of mother and embryo as close together as possible without actually allowing them to mix. Its methods of formation are different in many mammals, but all entail a large amount of growth. Sometimes this is of a particularly interesting nature because the boundaries between the cells of the growing tissue may break down so that it grows as a solid sheet of protoplasm (known as a *syncytium*).

The amnion, allantois and placenta form no part of the embryo, but after the expulsion of the latter at birth, they come away as the "after-birth." While comparable in a general way with the seed and fruit of plants, these organs differ in that they arise from parts of the ovum, whereas the fruit and seed are part of the parent plant.

While the embryo mammal is growing within the womb, the latter must of course increase in size also to make room for it. In the human being it increases in volume from about 4 to 6000 cubic centimetres, and its walls are thicker in proportion. Its increase in weight is from 2 ounces to 2 pounds. The remarkable thing about the growth of the womb is that it is not caused by cell-division, but by the increase in size of the individual cells. All its tissues are involved in this growth, but especially the muscle cells, which increase to ten times their original length and five times their width. Another interesting point about it is that this growth is not permanent, and after the birth of the embryo it returns to its former condition. This process, known as involution, is due to the shrinking of the muscle cells to their former size without any reduction in their number.

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CHAPTER V

REGENERATION

Instances of growth are most often looked for in the development of an organism from the ovum, for the young is smaller than the adult and the phenomenon of development is attended by considerable increase in size. But the ovum and the embryo are not the only things that grow: power of growth is not lost when the organism has grown up and reached its adult form. Indeed, in a sense, plants can never be said to be "grown up" owing to the possession of the growing point.

The processes of life, metabolism and the expenditure of energy in growth and movement entail a continual breaking down of the tissues of an organism, and these must be replaced if the organism is to continue to live. This *physiological regeneration*, as the process of repair is termed, goes on throughout life, and it is the failure of this power which is the cause of true death by old age or senile decay. It takes place by means of cell division but does not bring about any increase in size.

Stentor is one of the single-celled animals, or Protozoa, and possesses a ring of cilia (like little hairs) round its mouth. When this is "worn out" it is replaced by another ring and cast off.

In crabs and lobsters a periodical shedding of the external hard shell takes place, followed by its replacement by hardening of the underlying skin. In these animals this process appears to be in part a method of getting rid of waste products, since these are elaborated into the shell and accumulated there until got rid of.

Among the "moss animals," or Polyzoa, a regular occur-

rence is for part of the organism, with the nervous and alimentary systems, to disintegrate into a shapeless mass of decomposing substance known as a " brown body." At the same time a new alimentary and nervous system is produced by growth and the organism is reconstituted by regeneration. This is a very convenient method of " doing up " the organism.

In vertebrates it is found that different tissues have different powers of regeneration. The skin in mammals is composed of two layers, an external horny layer (*stratum corneum*) and an underlying layer of cells rich in protoplasm and capable of growth (*stratum malpighi*). The outer horny layer is continually being worn away and rubbed off at the surface and replaced from below by division of the cells of the stratum malpighi. Nails, hairs and feathers, which are modifications of epidermal tissue, show a similar power of replacement and growth throughout life. The growth from the base of a nail is a familiar phenomenon, as is that of a hair or a feather, and the replacement of the latter after moulting needs no emphasizing. In all these cases there is an actively growing base consisting of cells rich in protoplasm, with an abundant blood supply, which grow and divide and thus add to the length of the overlying structure from beneath.

In the lower vertebrates, from the fish to the reptiles, the teeth are constantly being shed as they are worn out and replaced by others which develop in the gums beneath them. In the mammal this replacement normally takes place only once, resulting in the acquisition of the permanent dentition after the loss of the milk teeth. In some forms the permanent teeth have in addition the power of growing throughout life. Their possessors are animals whose food requires grinding and this entails a continuous wearing away of the surface. This shortening of the tooth at the crown is compensated, as in the horse for example, by continuous growth at the root.

The antlers of deer furnish an interesting example of

periodical shedding and replacement, all the more remarkable because of the large size of the structure restored and the comparatively short time taken by the process of regeneration. The antlers are shed every year, and each year the regenerated antler is larger than the one of the preceding year until the stag is full grown.

Glands, whose secretion is composed of cells set free, must be included with the tissues which are capable of cell division. Perhaps one of the best examples is that of the red blood corpuscles, which are continually being produced in the marrow of the bones and destroyed in the liver and elsewhere. The genital organs also, with certain exceptions, are capable of unlimited production of new cells.

All these tissues are continuously undergoing a process of cell division which is similar to what occurs in development and would result in growth and increase in size were it not that the amount of new tissue so produced corresponds exactly with the amount which is lost. They do not normally overstep this limit and thus the tissues are prevented from exceeding the specific size and form of the adult.

Other tissues do not normally get replaced, but may do so under exceptional circumstances. Little bone ordinarily grows after the adult stage has been reached, but after a fracture the two broken pieces of bone are soldered together by new growth.

Yet other tissues appear to be totally incapable of being replaced, and to these belongs the nervous system in higher forms, whose cells, although they are capable of regenerating their processes, are fixed in number at a very early stage of development, and do not divide and are not replaced if lost or worn out. In these cases it is probable that the inability to grow and divide is caused by the high state of differentiation reached.

In all the above-mentioned cases cells grow and divide without the organism growing any larger. But if as the result of an accident a part of the organism be lost, its replacement by regeneration will entail growth.

Many animals are capable under certain circumstances of detaching portions of themselves by their own effort. It is well known that if the common lizard be held by the tail the animal will free itself by breaking and detaching its tail, a phenomenon known as *autotomy*. After the loss the tail regenerates. The growth takes place from undifferentiated cells derived from the connective tissue of the stump. These proliferate and differentiate into the skin, muscles, connective tissue, fat and skeleton of the regenerated tail. The power of regeneration is not thereby lost, for if a regenerated tail be cut, it will again be replaced; full differentiation is not reached however.

In the same way crabs are prone to lose their appendages, legs and feelers by autotomy, and after healing over of the wound a new appendage grows.

A newt is capable of regenerating its limbs. The first step is the closing over of the surface of amputation by growth of the epidermis, which thus heals the wound. It is probable that the epidermal cells divide as a result of the stimulus caused by the wound. At the same time the muscles of the stump lose their differentiation. The nuclei of some of the fibres divide by the simple (or *amitotic*) method and there is formed a mass of undifferentiated cells at the tip of the stump constituting a bud. It is not certain whether this bud is derived entirely from the products of dedifferentiation of the elements of the stump, or from a division of small cells which have remained in the tissues without becoming differentiated (*archæocytes*). At any rate, the regenerated limb is derived from embryonic cells which grow and differentiate. The skeleton of the regenerated limb grows in much the same manner as in ordinary development.

The amputation of the limb will have entailed the severing of the nerve fibres innervating it. When the processes of the nerve cells are cut, that part which is separated by the cut from the bodies of the cells (in which lie the nuclei) degenerates. The cell bodies thereupon

regenerate the processes which grow down into the limb and innervate it.

The power of regeneration becomes reduced in the most highly-developed animals until in the mammals it is limited to the healing of a wound without restitution of the missing part. Similarly the power of regeneration decreases with age, for whereas a tadpole will regenerate its limbs or its tail, the adult frog cannot.

In the lower invertebrates almost any structure can be regenerated. Any piece of a protozoon containing a portion of the nucleus will regenerate. A whole Hydra can be reconstituted from a very small piece. In the sponges an organism may be completely broken up by forcing it through a sieve, which results in separating individual cells and groups of cells. Nevertheless, such isolated fragments are capable of regenerating a complete sponge, provided that some of the simple cells of the skin are present. The isolated fragments first become aggregated together, then follows a period of reorganization and re-establishment of regulation followed by redevelopment. It is an interesting fact that there is in sponges a particular kind of cells (provided with " collars " and therefore called " collar cells ") which by themselves are incapable of growing and differentiating into a new sponge. They become aggregated and form spheres which live for a considerable time but do no more. The collar cells do not appear to be capable of dedifferentiating into the embryonic condition necessary for growth. In some cases, as in sea-urchins, an isolated cell from the " blackberry " into which the ovum has divided, can produce perfect young animals. This is really a case of regeneration, for the cell is making up what is missing.

In most worms a head or tail can be regenerated according to which is cut off, and if a worm be cut into a number of little pieces, each will regenerate a head and a tail. In many species the various organs of the body occupy a definite position in particular segments counted from the anterior

end. A definite number of segments may be specialized into a head region. If a number of segments smaller than that of the segments of the head region be removed, that number will be regenerated. But if a larger number of segments be removed, the typical number of head segments is restored, and the rest of the body undergoes reorganization to conform to the relations of the new head. This is a very good example of regulation, the process which maintains the shape of animals, and into which it will be necessary to go more deeply later.

The flat-worms are a valuable group for the study of regeneration. Pieces cut from the end or middle of a Planaria can reconstitute a normal individual of small size. Or an animal bisected down the median line will regenerate the missing half. Under the stimulus of the wound the cells of the cut edges dedifferentiate and grow into the missing part, head or tail as it may be.

In cases where the piece which is to regenerate is devoid of an alimentary canal and therefore incapable of ingesting and assimilating new material, regeneration takes place at the expense of the existing material of the piece. In Bipalium (another flat-worm) the regeneration of the anterior and posterior ends is accompanied by a reduction in width of the original piece, so that while growth occurs in one direction there is reduction in the other and as a whole there is decrease rather than increase in size. This process (known as *morphallaxis*) is interesting as showing that the protoplasm tends to regulate itself into the form of the typical Bipalium, and that the consequent growth and differentiation is independent of assimilation of new material. When the organism is fully reconstituted and has a functional alimentary canal it will grow to the typical size.

Another common example of regeneration is to be found in the starfish, which can replace any arms that are missing, and it is common on the seashore to find animals with some arms regenerating.

Usually as much is regenerated as was lost, but this is not

always the case. The limitation of growth to the attainment of the size and form characteristic of the species is another instance of regulation. If for any reason conditions are not quite normal there will be abnormal results. Too little or too much may be regenerated, and in some cases the "wrong" organ. Thus a piece of the stem of the hydroid Tubularia, bearing a polyp may grow another polyp at the other end of the stem. Or the anterior end of a piece out from a worm may grow a tail instead of a head. In crabs the amputation of an eye (which is carried on a stalk) is followed by restitution of an eye provided that the optic nerve centre be not removed by the amputation. If it is removed, there will be regenerated not an eye but a limb. The development of the stalked eye is therefore conditioned by the presence of the optic nerve centre. These *heteromorphoses*, as these "mistakes" are termed, show that normal development and regeneration require normal conditions, and that changes in the conditions bring about abnormal results. Cases of more striking abnormality will be dealt with among abnormal growths.

Regeneration also occurs in plants. The replacement of a stem by modification of another or activation of a bud is not true regeneration, but a change in shape of existing structures. Regeneration occurs only when the new growth takes from the surface of amputation.

A common phenomenon in plants, when a piece of a stem is cut and deprived of its buds, is for an outgrowth of cells to occur forming a cap (or *callus*) which covers the cut surface. These cells originate principally from the cambium which in the normal plant is an embryonic tissue and devoid of much differentiation. The cambium cells proliferate and exude from the surface of amputation in the form of a ring; they may also increase greatly in size. The ring then spreads over the cut surface, and some cells may be contributed to it from the central pith and cortex of the stem, neither of which tissues are highly differentiated. The whole callus is a shapeless structure composed of embryonic

cells, and resembles froth coming out of the neck of a bottle. Here and there on the callus buds arise which grow into shoots and in this manner produce new stems. At the same time, at the other cut surface, a cap forms which will give rise to roots.

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CHAPTER VI

ASEXUAL REPRODUCTION

Although for an individual to arise from an ovum is the usual method of reproduction, in a large number of groups of the Animal Kingdom there occurs a process of growth from groups of cells without fertilization, resulting in the formation of a bud which gives rise eventually to a new individual. In some cases these individuals may become detached from the parent or stock, in others they will remain attached and produce a colony. From the analogy existing between this process and the growth of buds in plants asexual reproduction is also termed *vegetative* reproduction.

In budding the new individual is at the start small compared with the stock which gives rise to it. There may also occur a division of the existing organism into two or more equal or unequal parts by fission, and these products of division will then grow and differentiate into new individuals. This process entails what might also be called regeneration, and for this reason it is sometimes difficult to distinguish between asexual reproduction and regeneration.

Those forms which are colonial often give rise to a tubular outgrowth or *stolon* which at intervals produces a bud. This grows into an individual, which, remaining fixed to the stolon, adds to the size of the colony.

A familiar example of budding may be found in the fresh-water polyp Hydra. At the side of the animal there occurs a rapid proliferation of cells which have remained in the embryonic undifferentiated condition. As the bud increases in size it differentiates into a typical Hydra, remaining

adherent to the stock until completely developed, when it detaches itself. Should the bud not detach itself, a compact colony would ensue, as, for example, in the sea-pen Pennatula.

The medusa of the common jelly-fish, Aurelia, rises by constriction from a hydra-like individual, a process known as the *strobilization of the scyphistoma.* A number of medusæ are constricted off from the stock one below the other, in much the same manner as a number of circular slices of bread can be cut off from a cylindrical loaf. These medusæ detach themselves and grow.

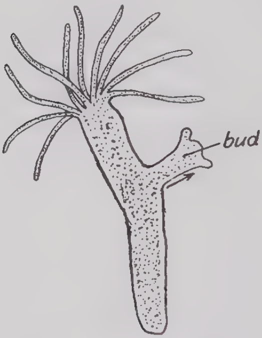

FIG. 19.—Hydra with a bud growing out of its side.

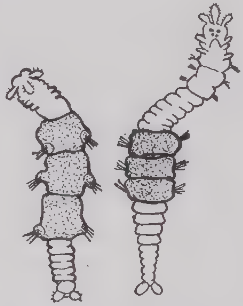

FIG. 20.—Two regenerating specimens of the worm Procerastea. The three segments which formed part of the original worm are shaded. They have regenerated a head in front and a tail behind. (After Allen.)

Among the flat-worms, *Planaria dorotocephala* is normally in the habit of undergoing division by transverse fission. The original anterior end grows a new tail and the posterior portion a new head. This reconstruction is hardly to be distinguished from regeneration.

Ctenodrilus is a small worm which breaks up into a number of short pieces, each containing anything from one to six segments of the original worm. When they are detached these pieces grow new heads and tails and reach the normal size. In this case there are zones of actively dividing cells which give rise to the new organs by proliferation.

Procerastea behaves in a manner somewhat similar to Ctenodrilus, but it is especially interesting because of the fact that the isolated pieces regenerate the correct number of segments in front and behind so as to leave the detached segments in the same position in the new individual as they occupied in the original worm.

The isolated pieces cannot assimilate new material until a mouth is formed together with the new head. In other forms, however, the new individual is perfected, so to speak, before being detached, and can assimilate and grow all the time. Autolytus is a marine worm in which the reproductive organs are confined to the posterior half of the body. This will separate from the anterior end, but before doing so in some species it produces a head. The anterior portion of the original worm grows at its posterior end and produces a number of segments equal to that which has been lost. For this purpose a budding zone appears just in front of the regenerated head of the posterior individual, and therefore in the middle of the original worm, a position which it would not ordinarily occupy.

In other species (*Myrianida fasciata*) there is no actual transformation of part of the body of the original worm to form the posterior detached individual, but the budding zone in front of the last segment (its normal position) proliferates very actively and produces a number of segments the anterior of which develop into a head. Just in front of this head the budding zone produces another set of segments, which likewise develop a head anteriorly. This process continues until there is a chain of thirty or more young forms, all with heads, of which the hindermost is the oldest, and all attached to the stock. Eventually they break loose and grow.

In plants asexual reproduction is very common. Only one example will be given here, viz., that of the leaf of the Begonia. A whole plant may be produced from a leaf or a piece of a leaf. What happens is that one or more cells of the skin of the leaf lose their differentiation and become

embryonic. They divide and give rise to a bud composed of small cells which grows into the new plant.

Enough will now have been said in this chapter and the preceding one to show that growth is not limited to the development of the young from the ovum. In the various groups of the Animal Kingdom there are to be found animals whose cells in particular regions are capable under certain circumstances of starting away on their own and producing either a new part in the case of regeneration or a new individual by asexual reproduction.

It is important to observe that in these cases there is growth of a particular region which had already reached the adult condition. Growth takes place by means of embryonic cells which have either lost their differentiation or never had any.

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CHAPTER VII

ABNORMAL GROWTHS

Development is a normal and regular occurrence in all the individuals of a species. If asexual reproduction occurs at all in a species, all its individuals may reproduce in this manner, which will be normal for the species. Regeneration can be said to be a regular occurrence in a species, but it requires as a preliminary the loss of a part, or a wound, and if it occurs at all in a species all its members will have the same capacity for doing so. Regeneration may therefore be said to be of common occurrence in such a species, and to result in the restoration of the normal condition of the organism.

There are some kinds of growth, however, which play no part in the normal life-cycle of an organism, but rather the reverse, and among these abnormal growths may be mentioned galls in plants and tumours in animals.

Plant galls are malformations due to irritation caused by parasites. A particular species of parasite produces a definite kind of gall on a particular species of plant ; that is to say, that the stimuli given to the plant by individuals of one species of parasite are all identical and produce the same result on the plant. The individuals of another species of parasite will produce a kind of gall different from the first, but its form will be constant for that species.

The parasite by its presence or by introducing toxic substances into the plant tissues by stinging, etc., stimulates growth on the part of the plant. In some cases it may affect only the epidermis, some cells of which grow

to enormous size (*Eriophyes macrochelus* on *Acer campestris*). At other times only the underlying tissues are affected.

Some galls are produced by huge increase in size of the original cells without their multiplication (*Oligotrophus solmsii* on *Viburnum lantana*). Others arise by cell division in a particular tissue (*Pemphigus bursaria* on *Populus nigra*). The tissues in the gall may be more or less devoid of differentiation or they may show traces of the differentiation of the particular region of the plant in which they are situated.

Stimulation of the epidermis may give rise to "hairs" of large size. In *Potentilla tormentilla*, attacked by the fungus *Synchytrium pilificum*, the epidermis produces long hairs, while the underlying tissue proliferates into a swelling. The parasites live within the cells of the swelling, and it is interesting to see that the neighbouring epidermal cells are stimulated to grow by "infection" at a distance. There will be more to say later about how growth may be brought about by action at a distance.

By vigorous growth of the superficial cells of a small area a sac-shaped hollow protuberance arises within which the embryos of the parasitic insect develop.

A familiar kind of gall formed on apple trees and consisting of irregular bulbous swellings round the stem and at the bases of the branches is brought about by parasites which remain on the bark of the trees, and therefore give it permanent irritation.

There appears to be no single method of formation of a gall, but different kinds of stimuli are given by the different parasites. In some, such as the saw-flies, an irritant is injected which causes the proliferation, and the gall within which the embryos develop. In the gall-flies (which are responsible for the formation of the familiar oak apples) no irritant is injected through the sting when the ovum is laid, but the gall develops in response to the presence of the larvæ.

The fact that there are so many different kinds of stimuli accounts for the great diversity of types of galls produced

PLATE IV.

[From Drew.

FIG. 21.—Tissues growing *in vitro* with cells dividing normally.

[From Drew.

FIG. 22.—Kidney tissue grown *in vitro* and dedifferentiated. All the cells are alike and devoid of special structure. Compare Fig. 23.

by even closely allied species, and on the same plant. One of the most interesting cases of this specificity is afforded by the gall-fly, *Neuroterus lenticularis*. This species has two generations during the year, one arising from a fertilized ovum, the other from an ovum which develops without being fertilized, or, in other words, parthenogenetically. The latter differs in certain structural details from the former and was for some time thought to be a separate species and named *Spathegaster baccarum*. Both generations lay their ova on oak leaves, those of Neuroterus produce round sappy galls, those of Spathegaster hard lens-shaped ones. The fact that the galls are produced at different times of the year when the trees are presumably in different conditions may account for their dissimilarity.

Mention must be made of *Rozites gongylophora*, a fungus which is carefully cultivated on specially produced manure beds by the leaf-cutting ant (Atta) in Brazil. Ordinarily this fungus produces spores, but under the treatment to which it is subjected by the ants it grows into white swellings which are used by the ant as food.

The actual manner in which the gall-producing stimulus works on the tissues is unknown, and attempts at the artificial production of galls have not been successful. The effect of simply pricking and wounding tissues can, however, produce growth phenomena, and this will be referred to again in connexion with growth-promoting substances.

In animals irregular and abnormal growths are tumours. Ordinarily the tissues do not grow any more when they are differentiated and the adult condition has been reduced. But under certain circumstances cells may start off growing on their own and give rise to swellings. They may form in connexion with any tissue, and may resemble the tissue from which they spring in type of differentiation of the cells. In such cases, from the fact that the cells have a certain amount of differentiation, they grow more or less slowly and are known as innocent or benign tumours in human pathology. As a rule the organism reacts to such

a structure by enclosing it in a capsule or case. This is a common reaction on the part of organisms to foreign bodies, and is responsible for the production of pearls in oysters.

The tumour arises from certain cells which for some reason have dedifferentiated and acquired energy to grow, but in the case of benign tumours the dedifferentiation is slight. In the case of the epidermis which is capable of cell division throughout life certain stimuli may give rise to local proliferations, the results of which are warts.

In other cases the dedifferentiation of the cells composing the tumour is complete. They divide and grow rapidly as a shapeless mass of embryonic cells, regardless of their position in the animal, the functions which they used to perform and the inconvenience caused by their action. They are usually devoid of nerve supply and they grow at great speed. Attempts at encapsulation by the animal are frustrated by the tumour invading the tissues bordering on it. Such a tumour is termed malignant and constitutes the most redoubtable form of cancer. Not only is the abandonment by the cells of their former functions deleterious, but their invasion of other tissues, and the mechanical disturbances produced by the presence of a large mass of tissue in undesirable positions, is dangerous to life.

In some way these cells are stimulated and released from the normal regulation which keeps the cells of the normal body in order. As they grow, which they do in all directions, they form a structure which appears to have a separate individuality of its own, and which goes on growing even after being transplanted into another animal. When the placenta does not cease growing at the birth of the embryo, it gives rise to a tumour. Presumably the factor which normally inhibits its growth when its function is no longer required, is absent.

In the case of a tumour of the ovary, the growth arises from cells which normally are destined later to have an individuality of their own and to grow extensively. Some

interesting experiments bearing upon this subject have been made. A fertilized frog's ovum can be made to grow when planted inside the body cavity of an adult frog. The results of its growth depend on various circumstances such as the age of the ovum and the region where it is planted. It may attempt to form a very imperfect embryo, or the products of its division may separate into little individual groups without much differentiation, and which invade the tissues of the host, thus resembling malignant tumours.

These abnormal results are of course due to the abnormality of the conditions to which the implanted ovum is subjected, and which upset the process of regulation.

It is obvious that there is great developmental energy in the ovum, and that if the directive and regulatory influences controlling its development and maintaining its form are interfered with or destroyed, great abnormalities will result. The same explanation probably applies to tumours, a break-down of regulation and the acquisition of growth energy being responsible for their formation.

A kind of growth which may be called abnormal, since it occurs in artificially produced conditions, may be seen in experiments of tissue culture. By taking small pieces of tissue and keeping them sterile and aseptic in nutritive solutions in small glass vessels, it is possible to keep them alive indefinitely and to make them grow. The nutritive media may be composed of the plasma of the blood of the animal, or lymph, or a specially prepared solution of inorganic substances. Few things are more striking than to see living tissues growing like this in little glass vessels.

Tissue culture, or growth *in vitro* as it is also termed, has already given results of the highest importance. It was seen that certain tissues in the living organism are incapable of any growth or regeneration after a certain stage in development, nevertheless such tissues may be made to do so in vitro. Although the circumstances are abnormal and the tissues would ordinarily not have grown, such growth in vitro is normal in so far as the cells grow

and divide by regular cell division in precisely the same manner as they would in the organism.

The method is also of the greatest value for testing the effects which various tissues have on each other's differentiation, and the effects of various substances and physical agents (such as X-rays) on growth.

A piece of kidney in vitro will dedifferentiate and grow as a sheet of embryonic cells. Apparently the very act of separating a piece of tissue from the "control" exerted by the rest of the organism results in loss of differentiation. If, then, a piece of connective tissue be added to the culture, some of the kidney cells will redifferentiate into the tubules characteristic of the structure of the kidney. In the same way a culture of carcinoma (cancer) of the breast produces an undifferentiated mass of cells, but the addition of connective tissue causes the formation and redifferentiation of mammary glands. In some cases, pieces of tissues grown and dedifferentiated in vitro can be made to redifferentiate after being grafted back into the organism, when they cease growing.

Altogether, tissue culture is one of the most valuable methods for prying into the secrets of growth and differentiation.

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PLATE V.

[From Drew.

Fig. 23.—Redifferentiation and formation of tubules by introduction of connective tissue into a culture such as is shown in Plate IV, Fig. 22.

[From Simpson, *Q. J. Exp. Phys.*

Fig. 24.—The effect of thyroid on growing sheep. The thyroid of the animal on the left was removed at an early age.

CHAPTER VIII

CAUSES AND NATURE OF GROWTH

Having surveyed in a general way the field in which growth is to be found, and observed that it consists in increase in size by various means, but principally by the creation of new living matter, it is time to ask, what does the pushing? This is almost the same as asking why protoplasm is alive, for growth is the creation of life. Protoplasm is constantly metabolising and changing the atoms and molecules of its substance, taking up fresh ones and letting go of others. It is like a whirlpool which involves now one particle of water, now another. At no time can it be said that it consists essentially of any particular portion of matter, for the essence of the whirlpool is the "whirl."

But life is no ordinary whirlpool because it is self-perpetuating, the clock winds itself up. To say that living matter assimilates foreign substances and builds them up into matter like itself, and subdivides to produce forms similar to the form that produces them, is to give a working definition of life derived from observation, but it explains little.

Recent work in an altogether different field of research, viz., in genetics, has revealed the presence of entities which are self-producing and self-perpetuating *par excellence*. These are the hereditary factors responsible for the production of the various characters of the organism, now well known as *genes*, or Mendelian factors. Genes are carried in the nuclei of cells, and it is through the genes in the nuclei of the reproductive cells, ova and spermatozoa that

the similarity between one generation and the next is brought about. In other words, genes are the basis of heredity.

Now, genes work upon the general internal condition of the organism, and the effect which they produce is in relation to that condition. Since growth is one of the main properties of an organism, it is not surprising to find that genes affect growth also. Indeed, there is a gene in the fruit-fly (Drosophila) which when present so disturbs the normal condition of the fly that it induces it to grow tumours. Yet other genes affect growth in a more normal manner. Why does one race of peas grow to a height of six feet and another to only one foot? Breeding experiments have shown that these two races differ by one gene. This is expressed by saying that the tall race has a gene for tallness and the other one for dwarfness. Since the height to which the plant grows must be the result of its general condition, it follows that the genes must work by producing a change in that general condition.

It has been known for some time that crosses between different races of animals produced offspring which are of greater size and vigour than those produced by a mating of closely related parents. This is often spoken of as the beneficial effect of outbreeding and the harmful result of inbreeding. Now this difference can be explained by means of genes, though the explanation would lead beyond the scope of this book. It must suffice to say that as the different races have different genes, the hybrid produced from them will have more genes than the thoroughbred derived from a pure stock in which the genes are alike in both parents. The more genes there are the greater the vitality and growth of the organism. This matter has just been mentioned in order to bring out the important point that growth has a genetical aspect as well as a general physiological one.

In order to start growing most ova require a stimulus of activation by fertilization. But others, if unfertilized,

will take to developing parthenogenetically, as in the bee; others again normally develop without fertilization. Spores of plants such as moulds and fungi always germinate without fertilization. It is probable, therefore, that the initiation of development is not due to the acquisition by the ovum of some matter or energy which only the spermatozoon can supply, but to the removal of some inhibition, which the parthenogenetic ovum is able to do for itself. The first inhibition to be removed is the influence of the rest of the body and the regulation which inhibits growth. This is normally achieved by detachment, the ovum leaves the ovary and is laid. And while this with suitable conditions of temperature and moisture is sufficient for the spore and the parthenogenetic ovum, the ordinary ovum requires something more. Experiments which have succeeded in inducing eggs normally requiring fertilization to develop (by artificial parthenogenesis), suggest that the surface membrane of the egg is made more permeable to ions, substances in solution carrying electric charges. In fertilized as well as parthenogenetic ova, both natural and artificial, there is an increase in the rate of oxygen consumption from the moment of fertilization or induction of artificial parthenogenesis when the ovum develops. The ratio of the volume to the surface of the ovum is large, and increase in activity of the protoplasm must be accompanied by increased facility of communication between the interior and exterior, for the larger a body is the less surface will there be in proportion to its contents.

The whole array of instances of regeneration, asexual reproduction and abnormal growths lend support to the view that growth takes place as a result of a fundamental capacity of living matter whenever it is not prevented. True growth entails increase of living matter, and since the principle of conservation of matter and energy holds good for organisms, the new material must be derived from somewhere. In regeneration in some cases (where morphallaxis occurs), it is derived from the other tissues of the

organism which thereby undergo reduction, in development it is derived from the yolk of the ovum and the starch of the seed, and then by captured food.

An insight into the nature of the chemical processes which accompany growth may be obtained by considering the conversion of reserve material for germination in barley. Reserve material is stored in the form of starch, but before it can be utilized it is converted into sugar by the action of a ferment or enzyme, diastase. An enzyme is a substance which by its presence accelerates a reaction, remaining unchanged at the end of it, and thus has similar properties to the catalysts of chemistry, about which there will be more to say. It is probable that the further elaboration into protoplasm takes place by means of other enzymes, all these processes going on within the cell. The processes attending the elaboration of yolk are unknown, but there can be no doubt that they also are the result of the action of enzymes.

When the young organism, seedling or larva is old enough to feed itself its store of reserve material is exhausted. Plants assimilate simple substances which are of universal occurrence all over the world. They depend for their nourishment on two sources, the air and the ground. The air contains carbon dioxide, and with the help of the green pigment chlorophyll and the energy of sunlight the carbon is fixed in the leaves and the oxygen set free. The air is, of course, the source of supply of oxygen which is necessary for respiration. From the earth the plant derives water and the simple salts of the soil in solution, through its roots. The carbon in the leaves is combined with water and elaborated into starch, probably passing through an intermediate formaldehyde stage. Protoplasm on analysis (and therefore necessarily when dead) yields the properties of that body of chemicals known as the proteins and breaks down further into amino-acids. It is probably through amino-acid stages that the products of assimilation are elaborated into protoplasm.

Animals cannot take in the simple substances which satisfy the requirements of plants. In addition to salts and water they require proteins, carbohydrates (flour, sugar) and fats. These chemicals are not found in the inorganic world, but only as products of life in animals and plants. Animals require food which has been alive and consequently all animal life is dependent directly or indirectly on vegetable life. The proximal constituents of food (as the classes of chemicals enumerated above are called) are ingested and by various means rendered capable of passing through the lining of the alimentary canal, and this process, which is achieved by enzymes or ferments, is digestion. The substances digested are carried by the blood to the various parts of the body and elaborated into protoplasm.

By experiment it is possible to find out which are the substances without which an animal cannot live or grow. These, then, will be the necessary raw materials for growth. Among them are to be found iron and iodine. Carbohydrates and fats, however, are not essential since they can be formed from protein food. As has just been seen, amino-acids represent a stage in the building-up of proteins, and some of these acids are essential, while others appear not to be. It would, however, serve no useful purpose to enumerate them and to go into the details concerning them here. It might, however, be mentioned that although several of these acids are necessary both for growth and for maintenance of life (apart from growth), others (lysine) are essential for growth but not for maintenance.

After development has ceased and the adult condition has been reached, assimilation continues to provide energy and to make up for the wear and tear of the tissues through use.

Growth, then, is a fundamental property of living matter, intimately connected with the self-perpetuating nature of the processes of life itself.

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CHAPTER IX

SUBSTANCES WHICH SPEED UP GROWTH

Some diets which are adequate for the maintenance of adult animals will, however, not permit of growth. Rats have been fed for 530 days on a diet of a substance called gliadin without difficulty, but young rats fed on this diet will not grow. In a similar way, a diet deficient in some particular substance will arrest the growth of a tumour while satisfying the needs for the maintenance of the animal. If, however, the young rats fed on gliadin alone, for a time longer than their growth period, are replaced on a normal diet, they resume their growth where they left off. This means that the animals will grow at a time when normally they would have long ceased growing and that their tendency is to grow provided that they are not prevented. Kittens under anæsthetic do not grow, but start again when normal conditions return. There is prompt response to the opportunity of resuming growth at all sizes. Tadpoles, however, are not affected in their metamorphosis and development by narcosis and anæsthetics.

The so-called accessory food factors now come for discussion. It has been known for some time that synthetically pure diets containing the correct quantities and proportions of the proximal constituents of food, produce certain diseases. Lack of fresh milk produces rickets, a diet of rice which has been polished, and therefore without the skins, gives rise to beriberi, deficiency of fresh green vegetables cause scurvy. These diseases are cured when the correct food is taken, and these substances which are necessary for the proper functioning of the body over and above

a diet adequate on the grounds of ordinary requirements are now familiar as *vitamins.* From the present point of view the interest of vitamins lies in the fact that they are essential for the growth of young animals. In their absence growth will not occur and speedy death may ensue.

Three vitamins have been recognized and called A, B and C, their absence being responsible for the three abovementioned diseases respectively. The principal sources of vitamins are green leafy vegetables, fresh milk, butter, beef fat, fruits and the oils of the livers of certain animals, the chicken and notably the cod, but in the latter cases they are derived from vegetable food so that plants are the ultimate source of vitamins. Vitamin A is soluble in fats, B and C in water, and these facts are sometimes made use of when speaking of them, as of "the fat soluble vitamin" for instance.

As to the nature of vitamins and what they are composed of, practically nothing is known. Their existence is inferred from their effects. From the fact that they exert their effects when present in only minimal quantities they are probably of the nature of enzymes.

In a similar way an extract of seaweed stimulates the growth of marine diatoms, and bacterized peat extract accelerates the growth of plants. In all these cases the effect produced appears to bear little relation to the amount of vitamin present. It merely just has to be there.

The foregoing leads on to the consideration of definite enzymes, chemicals secreted in the organisms by definite glands and producing a special result in certain parts of the organism. These substances are now familiar as *hormones*, the products of endocrine organs, organs of internal secretion or ductless glands as they are called. Hormones are poured into the blood by the glands which secrete them, and they are therefore taken all over the body: their name is derived from the Greek word "to excite," and since they are of the nature of chemicals, and exert their

actions at a distance from the place of their formation, they can be considered as "chemical messengers."

One of the best known hormones is that produced by the thyroid gland, which is situated in the front of the neck. Thyroid secretion acts as an accelerator of metabolic rate, of the speed at which the actions and reactions, constructive and destructive of protoplasm, take place. Insufficiency of thyroid in the developing mammal results in stunted growth, abnormal proportions and lack of development of the brain. This effect is very marked in sheep and goats, and in human beings this condition with its accompaniment of idiocy is characteristic of those unfortunates whose development is so imperfect, especially as regards the brain, that they are often called mentally deficient and cretins. Administration of thyroid to such cases results in the resumption of growth and normal development, one of the triumphs of modern medicine.

In the frog the thyroid is a factor in bringing about metamorphosis, turning the tadpole into the frog. In some respects it might seem that the frog was an unsatisfactory type with which to illustrate growth in animals, because of the complications involved in metamorphosis. As a matter of fact, however, this very feature is a point in favour of the frog since an analysis of the conditions underlying metamorphosis and its causes is very instructive from the point of view of growth.

Metamorphosis in the frog is characterized by the production and differentiation of certain organs and the reduction and disappearance of others. Investigations of the effect of thyroid secretion on the tissues show that those regions which are positively affected in metamorphosis react to the thyroid by a marked increase in the rate of cell division. This agrees with the general property of the thyroid to increase the rate of metabolism and the activities of protoplasm in general; but it is very interesting to see that it has a selective effect on the tissues, acting on some but not on others.

The increased rate of cell division results in morphological differentiation of those parts (limbs, tongue, lungs) which distinguish the terrestrial air-breathing frog from the aquatic tadpole. Metamorphosis is unaccompanied by any increase in size, but rather by a decrease as a whole.

By administering thyroid to young tadpoles it is possible to induce them to metamorphose much sooner than they normally would and the resulting frogs are quite tiny. Conversely, if the thyroid be removed from a young tadpole, it will go on growing and reach a huge size for a tadpole without metamorphosing at all.

The Mexican axolotl, a kind of newt, is an interesting

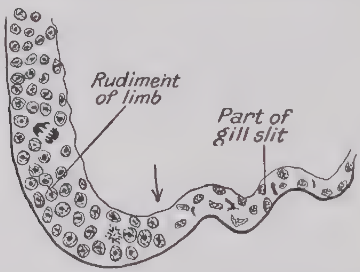

FIG. 25.—A portion of skin of a tadpole to which thyroid has been administered. There is a rapid cell division and growth in the region which will give rise to the limb, which region is sharply marked off (at the arrow) from the degenerating gill region. (After Champy.)

animal since according to circumstances it may or may not metamorphose. In the latter case it becomes sexually mature although structurally it is still in a larval condition with gills and open gill-slits. Administration of thyroid can also cause it to metamorphose into the adult form, Amblystoma as it is termed.

The thyroid is known to be connected with the metabolism of iodine, and it is found that tadpoles fed with iodine will metamorphose precociously. They will do so when fed on iodine even if their thyroids have been removed. This apparently puzzling result is due to the fact that the power of elaborating a substance with iodine which increases the rate of metabolism is possessed by the ordinary cells of the tissues of the body, and that the thyroid gland is

merely an organ which specializes in the elaboration of this product. One of the effects of metamorphosis in frogs is to produce a bulging out of the eyes, which, as is well known, are very prominent in the frog. It is an interesting and probably not unconnected fact that the diseased condition in man known as exophthalmic goitre should be characterized by protrusion of the eye-balls, for it is due to excessive activity of the thyroid.

Another ductless gland of great importance is the pituitary. This gland is situated under the base of the brain and just over the roof of the mouth. In mammals, excess of secretion of the pituitary is responsible for those disorders known as gigantism and acromegaly. These result in putting off the time at which the growth of the long bones normally ceases; these, viz., the limb bones and certain others, consequently grow to a greater length and the organism is larger than normal.

Tadpoles treated with pituitary grow to a much larger size before metamorphosing than they normally would. In spite of this increased size there is a slight acceleration of the time of metamorphosis. The pituitary therefore plays a part in metamorphosis as well as the thyroid, and this is shown very well from the fact that animals from which the thyroid has been removed can be made to metamorphose by administration of pituitary extract.

If a pituitary extract is injected into young rats, a great growth-promoting effect is obtained. For example, of rats 333 days old, those treated with pituitary weighed 596 grams, whereas the untreated ones weighed 248 grams.

The intricate interrelations of the ductless glands, of which there are about a dozen, brings it about that growth may be influenced by other glands besides the thyroid and the pituitary. The glands of the reproductive organs are antagonistic to the pituitary, and therefore tend to restrict growth. Conversely, castrated animals usually are larger and more lanky than normal. The glands of the reproductive organs in mammals are furthermore responsible

for the growth and differentiation of the distinguishing sexual characters. By grafting a male gland into a female the latter can be masculinized, and a male can be feminized by the converse graft.

There is no doubt that the ductless glands are of the greatest importance in controlling growth and differentiation, and it has been suggested that the various types represented by the different races of man owe their differences to variation in the strengths of the secretions of certain of the ductless glands. In this way some races have long noses, others short, some high cheekbones, other low, and hormones are known to affect the coloration of the skin.

A substance which has the power of promoting growth has been obtained from very young mice, and termed embryo extract. This substance encourages growth of pieces of tissue cultured in vitro. Extract of adult tissues prepared in the ordinary way by breaking up the cells and dissolving the contents has no effect upon growth. If, however, the adult tissue be first autolysed at body temperature (autolysis is decomposition of the protoplasm of cells), an extract from it has extremely powerful growth-promoting properties. Furthermore, this extract behaves upon tissues in vitro in the same manner as extract of a malignant tumour. It is possible, therefore, that the discovery of this autolysed tissue extract may have important results with regard to the discovery of the causation and treatment of cancer. This autolysed extract produces explosive growth of tissues for a short time and then ceases unless the culture medium be changed. It is possible that as cells break down owing to wear and tear they liberate some of this substance, which stimulates neighbouring cells to divide and replace them, and that their growth activities cease after a very short time, so that no more tissue is regenerated than was lost. It may be that the difference between cancerous and normal tissue consists in that the latter only have the autolysed substance as the result of

the breakdown of certain cells and that with them growth (repair, physiological regeneration) is rhythmical and conditioned by requirements, whereas the former appear to have the substance free.

The production of a growth-promoting substance from damaged cells accords very well with the evidence from plants. Galls probably arise in this manner. Wounding or destroying tissues may lead to growth of the injured or neighbouring tissues. Parthenogenesis may be induced in the ovule by pricking the pistil. It is the action produced at a distance by the presumable liberation of some chemical substance which has led to the suggestion that the latter partakes of the nature of a hormone.

During pregnancy in mammals the womb undergoes growth, by cell enlargement, and high vascularization. It appears that this process is governed by an internal secretion produced by the empty follicle in the ovary, out of which the ovum has been expelled. The follicle becomes glandular and is known as a *corpus luteum*.

In insects which undergo a complete metamorphosis inside a pupal case, the larva or caterpillar disintegrates and the perfect insect arises as a result of the division and growth of special groups of cells known as imaginal discs. It is found that their growth is conditioned by a substance produced in the head, an example of a hormone in invertebrates.

The formed tissue of the stem of plants after differentiation undergoes no growth with the exception of the cambium. At first restricted to definite regions in the vascular bundles, the separate strips of cambium are united, the intervening tissue becomes embryonic and thus completes the cambium ring right round the stem. This activation of the intervening regions suggests the effect of a hormone, and there is evidence that one is produced in the bast of the vascular bundles (probably in the companion cells to the sieve tubes). Small portions of isolated tissue of potato will not grow unless some bast be present. This is inter-

esting because it is the first indication of a hormone in a plant.

The matter presented in this chapter must necessarily be somewhat scrappy. The study of vitamins, hormones and other growth-promoting substances is still in its infancy. It will at any rate have become clear that the growth activities of protoplasm are subject to stimulation by various agencies. The three classes of such agents dealt with in this chapter are grouped together because they are all organic and produced by living organisms. The last two are produced within the very organism whose growth activities they regulate. In the next chapter only external conditions will be discussed with regard to their effects upon growth.

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CHAPTER X

THE EFFECT OF EXTERNAL CONDITIONS ON GROWTH

Every one knows the effect which the weather has upon one. The temperature, moisture and wind are all external conditions. In the same sort of way external conditions affect the life processes of all organisms, and in this chapter a few of their effects on growth will be considered.

Dealing first with the effects of chemical agents on growth, it is important to realize that species are adjusted to particular environments with their definite concentrations and relative proportions of chemical substances, in a very delicate manner. For aquatic animals one of the most important things is that the concentration of hydrogen ions should be correct, for the acidity of the medium is thereby determined.

In the absence of a particular element, say sulphur or potassium, the normal metabolism of the organism is upset and it shows defective growth. There are other substances (morphine, zinc sulphate) which, when used in sufficiently dilute solutions, are capable of accelerating the rate of growth. In higher concentrations, however, these substances act as poisons, and it is probable that when present in minimal amount their effect is produced by a slight irritation to which the organism responds and is thus stimulated to greater growth. The concentration must be within the limit of acclimatization of the organism for this effect to be produced, or it will of course succumb to the poison.

In the elongating zone of a plant unequal growth of one

side will give rise to a curvature. Suppose a chemical stimulus retarding growth to be experienced by one side of a root, that side will grow slower than the opposite one and the root tip will turn towards the direction whence comes the stimulus. When the tip points straight in this direction all its sides will be equally stimulated and it will grow straight. In this manner directive responses to stimuli, or tropisms as they are called, may be brought about. It should be remembered, however, that these results are probably due to more than one process and that they may be very complicated. The foregoing description only attempts in a general way to explain how the end result may be brought about.

The density of the medium exerts an influence on the growth of organisms. Under reduced atmospheric pressure the growth of plants is accelerated, and conversely it is retarded when the pressure is increased. But in animals reduced pressure may deprive the organism of its necessary supply of oxygen for breathing and thereby retard growth.

In water the concentration of salts in solution is responsible for what are known as osmotic phenomena. Passage of water through a membrane into an enclosed space (endosmosis) resulting in the expansion of the latter, is produced when the concentration of salts within the space is higher (hypertonic) than that of the medium outside, and when the membrane lining the space does not allow the dissolved substances in the space to pass out of it. Such a membrane, termed semipermeable, is that of the cell. In freshwater infusoria (animalcules) the concentration within the cell is higher than that of the medium, therefore water is continually passing through the cell membrane into the organism which would swell and burst were it not that a special mechanism is present to expel the superfluous water (the contractile vacuole). Sea water, on the other hand, has salts in solution which give it the same osmotic pressure as the contents of the cell, and in marine infusoria no osmosis takes place and there is no water-expelling appar-

atus. Any conditions favouring endosmosis within certain limits accelerate growth. On the other hand, exosmosis, the passage of water out of a space and its consequent shrinkage, retards growth.

Attention has already been paid to the part which absorption of water plays in the development of the frog and in the phase of elongation of the plant. In general a state of turgescence is necessary for vital phenomena and growth. The absorption of water activates the dormant embryo in the seed. Absence of water in some aquatic animals is followed by a process of desiccation and hardening, and in this shrunken condition the organism may remain in a state of suspended animation, only to blossom out again when moist conditions return. This phenomenon, called anabiosis, is found in single-celled animals, slime fungi, wheel animals and water bears, and is an adaptation to life in surroundings which are liable to dry up, such as ditches and ponds. They tide over the dry period in their shrivelled condition and return to more active life when the ditches fill with water again.

Light exerts an inhibitory effect on growth in plants. In the dark growth is much more rapid, the fastest growth in nature taking place just before sunrise; and for this reason gardeners encourage potatoes and other vegetables to sprout in the dark. The lanky condition of plants grown in dark conditions is known as etiolation.

The effect of light can be exerted through protoplasm at a distance, because if light is allowed to fall on the leaves of a plant the growing point is retarded in its activities although the light does not actually reach the growing point, which is protected by leaves. Light may also produce an effect later in time, for leaves developed in light differ in their greater thickness from those grown in the dark, and in the beech, for example, the light or dark during one year determines the production of thick or thin leaves the following year.

The effect of light on one side of a stem of some plants

results in the relatively greater growth of the opposite side with consequent bending of the shoot towards the source of light. The growth of shoots of plants in a room towards the windows is a familiar phenomenon.

In some Algæ, however, and in animals light has an accelerating effect on growth, which is due to rays at the violet end of the spectrum. Orange-red light is best for assimilation of carbon and therefore nutrition in plants; indigo blue light is the most effective in retarding plant growth.

X-rays inhibit growth by their lethal effects on dividing cells. For this reason they are used in the treatment of cancer, and prolonged exposure to them is dangerous since they prevent the activities of the cells in physiological regeneration. Under certain circumstances, however, they may cause growth by stimulating the cells to divide. This slight positive effect of a stimulus, followed by a negative effect of greater intensity of the same stimulus, is very common in vital reactions, and it has already been noticed in connexion with the beneficial effects of sufficiently small doses of poisons.

The manner in which X-rays exert their effect on living matter is unknown, but the probability is that they act on the nuclei of the cell.

The rate of growth is largely governed by temperature, and organisms grow faster in heat (up to a maximum) than in cold. In this way climate comes to have an important bearing on growth. In man the age at which puberty is reached decreases from high latitudes to the Equator. In some forms low temperature inhibits vital activities without otherwise affecting the organism. The ova of the worm Ascaris develop as long as the temperature is equable. Should they be placed in an ice chest all activities cease, only to be resumed again at the point where they left on their being returned to warmer conditions. This is another example of the tendency to prompt resumption of growth whenever conditions allow it.

The effect of temperature on vital activities is comparable to that which it exerts on simple chemical reactions.

That is to say, the speed of the reaction increases proportionately to the temperature and it is possible to speak of a temperature coefficient of growth. To reach any particular stage of development less time is required at high temperatures than at low ones.

Table Showing the Time Required to Reach the Different Stages of Development in the Frog at Various Temperatures (after Higgenbottom).

	Mean Temperatures.			
	60° F.	56° F.	53° F.	51° F.
Mar. 11	Egg	Egg	Egg	Egg
„ 20	Hatch	—	—	—
„ 23	External gills	—	—	—
„ 25	—	Hatch	—	—
„ 27	Internal gills	—	—	—
„ 28	—	External gills	—	—
„ 31	—	—	Hatch	Hatch
Apr. 4	—	—	External gills	—
„ 6	—	Internal gills	—	External gills
„ 10	Big tadpole	—	—	—
May 22	Metamorphosis	Big tadpole	Internal gills	Internal gills
Aug. 18	—	Metamorphosis	—	—
„ 28	—	—	Metamorphosis	—
Oct. 31	—	—	—	Metamorphosis

Flowing water, an electric current, and the force of gravity must be mentioned as affecting growth, for although they do not change the rate of growth, they are operative in determining the direction in which growth occurs, i.e. upstream, with the current, or with or against gravity.

Enough will by now have been said to show that growth, like any other processes, is not independent of surrounding conditions, but is liable to be modified by them to a greater or lesser degree. The normal organism can only be produced in a normal environment.

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CHAPTER XI

SIZE

Organisms considered by themselves are like maps without a scale, and it is most important to remember that they must not be considered apart from their surroundings if it is desired to gain a general aspect of their activities. Just as physical phenomena, such as the boiling-point of water, for example, depend on other conditions, in this case pressure or the presence of other substances in solution, so the form, function and activities of an organism have to be in relation with the surrounding conditions. The organism reacts on the surroundings and to achieve its delicate adjustment to them it must be in equilibrium with its external conditions. Some examples of this equilibrium relating to agents affecting the rate of growth have been discussed in the preceding chapter. Here attention will be paid to some physical conditions which prevail on earth and with which organisms must comply in governing the size to which they grow.

One of the first subjects to claim attention is the geometrical fact that when a body increases in size its volume increases faster than its surface. The ratio between surface and volume constantly decreases as size increases, and it becomes necessary to enquire whether there are any conditions governing this ratio, which by forcing the organism to conform to them will thereby govern its size.

In all the higher organisms living matter is divided into small administrative and functional units, the cells. Each cell is not self-sufficient, it depends for its life on a supply of food and oxygen which it derives from outside itself,

and since the only way into the cell is through its surface, a given surface can only deal effectively with the requirements of a given volume. If the volume is too large with regard to the surface the contents of the cell will suffer, and this will happen when the cell is too large. Consequently there is a limit to the size which cells may normally attain in any given tissue. A giant individual of a species differs from a dwarf not in the size of its cells but in their number. By halving the ovum of a sea-urchin before fertilization, it has been possible to obtain larvæ which are half the size of normal ones ; nevertheless, the size of the cells in both is the same, but the smaller larvæ have half as many of them. This fact is well shown in species in which there is considerable variation in size, such as the dog. The cells of the lens of the eye are of the same size in a Pekinese as in a St. Bernard, only the latter has many more. The cells of the growing points of large and small varieties of any species of plant are of the same size.

There is another aspect to consider. The volume of a cell is filled with protoplasm in which there is a nucleus ; that portion of the protoplasm apart from the nucleus is termed cytoplasm. Now it is found that the volume of the cytoplasm bears a certain relation to the size of the nucleus. In the normal development of the sea-urchin (or any other) larva the ovum has been fertilized and contains nuclear matter derived from the spermatozoon as well as the ovum. The amount of nuclear matter contributed by the spermatozoon is equal to that contained in the ovum, so that if this quantity is called n, the fertilized ovum will contain $2n$. If, however, the unfertilized ovum is made to divide (by artificial parthenogenesis), each of the cells to which it will give rise will contain n. Now one of these two cells can be " fertilized " by a spermatozoon (containing n), so that the embryo will at this stage consist of two cells, one containing n and the other $2n$ amounts of nuclear matter. Development proceeds and in the larva one-half of the body (derived from the $2n$

cell) consists of cells which are twice as large as those of the other half. The size of the cell is therefore in relation with the size of the nucleus.

At the time of cell division the nuclear substance resolves itself into a number (definite for each species) of bodies termed chromosomes. The size of a nucleus is proportional to the number of chromosomes which it contains.

Some other illustrations of the relations of nuclear volume to cell size are found in the giant varieties of some plants, Œnothera, Primula and Solanum, for example. It is found that the giant individuals contain double the number of chromosomes characteristic of the normal-sized individuals of their species and consequently they have twice as much nuclear matter. Their cells are larger and give rise to larger plants. Conversely, there is a dwarf variety of the freshwater shrimp Cyclops. Ordinarily the nuclei of the cells of this species contain twelve chromosomes, but the dwarf has only six.

If the size of the cell be too large and therefore the ratio between surface and volume too small, the balance can be readjusted if the cell divides. Then the volume will be halved, but the surface only slightly reduced in the daughter cells. This is what occurs in the division of the ovum, which is a large cell usually full of protoplasm and nutritive material (yolk). Division produces no increase in volume but only increase in surface. At the same time there is a manufacture of new nuclear matter, so that by the time when the "blackberry" has been formed, the cells have a suitable relation between volume, nuclear volume and surface.

These remarks, of course, apply only to general cases, and in some instances other factors come in to influence size. In the plant the first process of differentiation of the cells is the elongation produced by the absorption of water. In the formation of the ovum and its dilatation with yolk, in the muscle cells of the pregnant uterus, and in the expansion of cells in plant galls, particular agencies

are at work which bring about the increase in size of the cell and the alteration of the ratios without cell division.

The general fact remains that in the majority of ordinary tissues, the size of the cells being constant, all true growth entails cell division. This is why ability to divide on the part of the cells is so important a factor in growth.

Insects and crabs have a stiff external skeleton of chitin which is periodically cast off as a moult. Growth must therefore take place in the time between the casting of one skin and the hardening of the new one. It is found in a large number of cases that the linear dimensions increase in the ratio of 1 to 1·26 (approximately) at successive moults. This number is roughly the cube root of 2, and if each of the three spatial dimensions (length, breadth and depth) increases by this amount, the volume will be doubled at each moult. This result would be obtained if each cell divided once and gave rise to two, each of which grew to the same size as their parent cell.

It follows from the foregoing considerations that if the size of the cells of a species is constant and the individuals are equal in size, they must contain an equal number of cells. In the cases in which it is practically possible to count all the cells of an organism, viz., in the Nematode (thread) worms, wheel animals (Rotifers) and water bears (Tardigrades), this is found to be true.

Attention may now be turned to some of the physical conditions under which the organism as a whole has to live. All organisms are subject to the action of the forces of gravity, and their form and activity are conditioned by these forces, with due regard to the medium in which they live. As a tree increases in height it also increases in thickness. But for any given ratio of increase in thickness with which growth in height is accompanied there will come a time when the tree must fall owing to its own weight. This might be guarded against by the use of stronger material, a steel pillar will stand when one of iron will bend. In the tree, however, this is not done,

and wood is the only available skeletal material. The height of a tree is therefore definitely limited (at about 300 feet). It is an outcome of the fact already noted that in an enlarging body the different geometrical dimensions, linear, superficial and voluminal, do not increase at the same rate, and that therefore the body will not be in equilibrium to external forces at all sizes. This demonstrates the importance of scale of magnitude. All sizes of a particular shape are not equivalent. By adhering to the size which is best suited to their surroundings organisms show how they are governed by their relations with the environment.

The body of mammals is entirely supported by the legs. Increase in size raises the volume and therefore the weight as the cube of the linear dimensions, whereas the cross-sectional area of the limbs (the measure of their strength) increases only as the square. In small mammals the legs may be thin and the whole of the weight may be carried on the fingers, endowing the animal with agility. But in the larger mammals the increase in the weight of the body is so preponderating (and there is no available material other than bone), that the legs must be disproportionately thickened to remain efficient as supports. So the elephants and all mammals living and fossil of comparable size tend to have stout legs like pillars, the whole weight being carried full on the sole of the foot, which curtails their agility. A further increase in size would necessitate legs out of all proportion to the rest of the organism, and which would be so clumsy that it would be unable to move them. Here, then, is a limiting factor for size in mammals, due to gravity in an aerial medium. In a similar way a bird cannot be of a greater size than that which will allow its muscles to actuate the necessary wing surface to keep up its weight during flight. Condors appear to be at the limit of size and to have difficulty in flying when gorged with food. Ostriches and the giant extinct birds have overstepped the limit and cannot fly.

If the medium be changed, however, conditions will be altered. By Archimedes' principle, immersion of a body in a liquid diminishes its relative weight according to the density of the liquid. For this reason aquatic animals can attain a size impossible for land animals. Whales may be 85 feet long, and some fossil reptiles which were over 120 feet long must have lived in water.

Another force with which organisms have to deal is surface tension. This is one of the forces responsible for the production of a film or " surface " at the interfaces between media, as between air and water. This film resists attempts to deform it, and a certain amount of energy is required to break through it. Small animals, such as insects, will be quite safe on the top of a surface film, but if they break it in order to drink or to dive, they must be sufficiently strong to overcome surface tension if they are to get out again. As their absolute strength depends on their size, surface tension may be said to constitute a limiting factor for minimum size in small land animals which have anything to do with water, either in the way of drinking it or being submerged in it. A parallel case is presented by certain small marine worms which normally live attached to the under-surface of the surface film. By the violent action of waves it may happen that they are forced through the surface film and then cannot get back through it again.

Often limiting factors arise as necessary consequences of the habit of life of the organism. Crabs moult regularly and get rid of their hard external shell, which serves them as a skeleton. After the moult the crab is soft until the new shell hardens. The time required for its hardening is determined by its size. A crab as big as a sheep would have to spend all its life recovering from a moult. The shell-less period must be kept down to a minimum on account of the danger which the animal incurs from the attacks of enemies, and its liability to collapse.

In order to make up for loss of energy, as heat by surface radiation, a small animal requires relatively far more food

than a large one, because the ratio of its surface to its volume is greater. Man eats one-fiftieth of his weight of food per day, a mouse eats half its weight in the same time, and it follows that a mammal smaller than this would have to consume more than its own weight in a day, a quantity which it would not have the time to eat.

Respiration is effected in insects not by a heart-pump mechanism, but by conveying air direct to the tissues through fine tubes, the tracheæ, which open to the outside of the animal. Owing to the limits of the rate of diffusion of air through these tubes, the insect cannot exceed a certain size without impoverishing the oxygen supply to its tissues.[1]

Size may have an important bearing on delicate adaptation to a particular environment. When the wing surface of herons is compared with their weight, it is found that they have a considerable margin of safety for flight. This enables them to fly with heavy loads of materials for nest-building. The blood corpuscles of the African lung-fish (Protopterus) are so large that they may choke the proboscis of the tsetse fly attempting to suck its blood, thus securing partial immunity for the lung-fish.

This chapter has as its object to show that variations in size cannot take place regardless of other conditions. Within the organism the sizes of cells and of their nuclei are interdependent; outside the organism various physical necessities have to be fulfilled. The excessive size of the Dinosaurs, and of the antlers of the Irish elk was probably responsible for their extinction, for they must have exceeded the limits. It has been seen that there are a number of factors limiting the extent to which organisms may vary in the matter of size. It must be understood, however, that these factors cannot be held to play an active part in the actual regulation of size in the development of the organism. The factors in question here, by setting

[1] I am indebted to Mr. J. B. S. Haldane for this information and for his permission to use it,

bounds which must not be transgressed, are to be regarded as examples of the working of natural selection, by eliminating the individuals which are unfitted in the matter of the size to which they have grown. As the animals which grew too large, or remained too small, became extinct, only those which grew to a correct size, left offspring. Growth, therefore, has played an important part in evolution.

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CHAPTER XII

THE RATE OF GROWTH

Having described in the previous chapters the ways in which growth occurs, it is necessary to enquire into the relations which the process of growth bears to standards of measurement, for now that the qualitative aspect of growth has been considered, the quantitative, dealing with how much growth takes place in how long a time, is the next step in the study.

If growth is considered in relation to time, in other words the rate of growth, valuable results are obtained with regard to the process of growth itself. Owing to the difficulties which are encountered in accurately measuring the volumes of living organisms, growth is measured by increase in weight, for weight may be taken as an indication of volume, and increase in weight is roughly proportional to increase in size. The weights of an organism at different times during growth may be expressed in the form of a table, but the most convenient method of expression of these relations is in the form of a graph, for it is then possible to see the nature of the whole process at a glance. If the values of the weights are plotted vertically and intervals of time horizontally, the curve obtained will show the amount of growth which has taken place at any time. This curve is a characteristic one, often called sigmoid from its resemblance to an S, and of which there will be more to tell in a later chapter. For the moment it is to be noticed that the increase in size of the organism is at first slow, then fast and lastly slow again when the curve tails off to the horizontal, and growth

ceases. This, of course, is when the adult condition is reached.

The actual rate of growth is indicated by the angle which the curve makes with the horizontal. The steeper the curve, the more growth will there be in a given time. It is not always easy to estimate this angle correctly and consequently recourse is had to other methods. If the actual amount of increase in weight in any interval of time is plotted against time, a curve is obtained which rises first slowly and then rapidly, comes to a peak and then descends again, until when growth has ceased the increments are of course zero. In this curve the peak occurs at the time when the curve was steepest in the previous graph (total

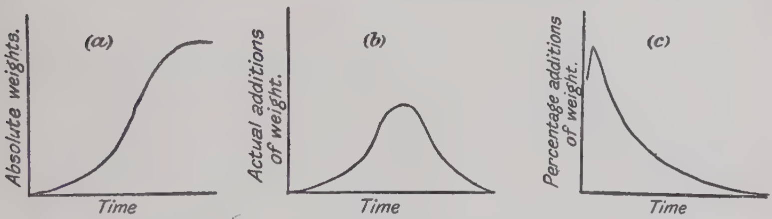

FIG. 26.—(*a*) Graph showing the typical sigmoid curve when the absolute weight of an animal is plotted against time. (*b*) Curve of the actual additions during a given space of time plotted against time. This curve is at its highest when curve (*a*) is at its steepest. (*c*) Curve of the percentage additions in weight during a given space of time plotted against time. This shows the slowing down of growth with age.

weight against time). This curve therefore shows the *actual additions* for given intervals of time, the amount which is added during any of these intervals at any time in the life of the organism.

On reflection it will be seen that although this curve measures the amount which is added by growth in any time, it does not convey a full impression of the rate of growth because it makes no mention of the amount of living matter already present which produces the increments. A large animal adding 1 pound to itself is obviously growing slower than a small one increasing in weight by the same amount. How is this to be expressed? What is required is the relative rate or percentage additions of growth in a given interval of

time. This is obtained by taking the addition in weight effected during an interval of time and expressing it as a percentage of the total weight of the whole organism at the beginning of that interval of time. This percentage plotted against time gives the curve of the *percentage additions* of growth. It gives a measure of the amount of living matter already present and the amount which it produces at any time.

The most striking thing about this curve is that the organism grows fastest when it is very young and that the percentage additions become less and less as it grows older. A small revival in the percentage additions occurs after about thirteen years in man, marking the onset of the changes of puberty.

At the age of one year (from conception) man is growing to three times his own size in a year, but even this high rate is less than that before birth. At four months the embryo is adding six times its own amount to itself in a month. This rate decreases until at birth the addition is only one-fifth of itself per month, which represents a percentage addition of 240 per cent. per year. Figures for the stages earlier than four months are hard to get, but there are indications that the maximum percentage addition is added at three months, before which there must be a very rapid rise in rate of growth, starting from the ovum.

If instead of man other animals are chosen as examples, such as the rabbit, or guinea-pig, chick, pond snail or sea-urchin, the same result is obtained. In the Protozoa, or single-celled animals, growth is practically synonymous with reproduction. The number of individuals produced in a given interval of time is, therefore, a measure of their growth. Plotting number of individuals in a culture against time, the number increases first slowly, then fast and then slowly again until the culture is " old," when it ceases reproducing. This is the characteristic sigmoid curve again. If the percentage increase in number of individuals is plotted, the

curve shows the continuous decrease in rate from an early high value.

In measuring the percentage additions of growth in a plant there are three points to be remembered. First, the growing point is a region which is permanently embryonic and it grows throughout the life of the plant. Second, there is the resting condition of the embryo in the seed to be considered, during which there is no growth. Last, growth in length in plants is effected chiefly not by production of new living matter, but by absorption of water. In the maize a curve of the percentage additions plotted against time shows the same general features as the curves just considered for animals. At first there is little increase when the plant is a seedling, before it has established proper connexion with its surroundings. Next follows a very rapid increase in growth rate and the curve rises almost vertically. It soon reaches a maximum, after which there is a steady decline, only interrupted by brief revivals in rate at the time of development of the male and female flowers.

Growth in regeneration with regard to rate gives the same result as in development: a growing tissue increases in size very fast at the start, reaching a high rate, which steadily decreases. In the regeneration of tadpoles' tails it is possible to plot a curve for *actual additions*, but not *percentage* additions, since it is impossible to define which weight should be taken from which to derive a percentage. Nevertheless, it is easy to see that the rate of growth rises very early to a maximum and that thereafter it falls steadily. With regard to time, therefore, growth in regeneration is identical in character with growth during development. There is a general deceleration of rate of growth with increasing age.

Increase in size can be due to more than one factor and it becomes interesting to enquire into the relative activities of these other factors at different times. In estimating the amount of increase due to absorption of water, it is possible,

by weighing before and after desiccation of the organism, to ascertain the amount of dry weight gained. This subtracted from the total weight gives the amount of water absorbed. In the tadpole, during the period of rapid growth, the content of water rises fast, whereas production of new protoplasm (increase of dry weight) is little. Later, the dry weights increase, showing that new living matter is being made, and the percentage of water falls. The same conditions hold good in man and in the chick.

In the growth of a plant the phase of elongation is due to absorption of water by the cells. Since the cells of the growing point are continuously dividing, the age of any particular cell increases with its distance from the growing point. It is found that the percentage content of water of the tissues rises from the growing point to the first internode. It rises more slowly from the first to the second internode, and below that remains constant. When the cells are distended with water they cease true growth, so that here, again, the rate of growth decreases with age.

Unequal growth in different directions and of different parts is responsible for morphological differentiation, and this unequal growth is brought about by unequal rates of growth. It has been shown that the action of thyroid extract on tadpoles in inducing metamorphosis causes an increase in rate of cell division, and therefore of growth, in certain parts. The different organs of one organism do not all grow at the same rate, and the curves plotted for each will differ from one another. Indeed, while some organs, such as the tadpoles' limbs, are growing fast, their tails exhibit negative growth and are resorbed.

A large number of the differences existing between related forms resides in differences of proportion of corresponding parts. Various regions and dimensions of one form may be proportionately smaller than in another. A simple example of the differences which may be produced by this means is to be found in the images reflected by concave and convex mirrors. Every one knows the tent at the fair, in which one

pays sixpence to see oneself distorted in such mirrors. In human beings these distortions may produce grotesque likenesses to the features of different people, and, in animals, similar transformations may produce likenesses to different species. That is to say, that such species differ in the relative

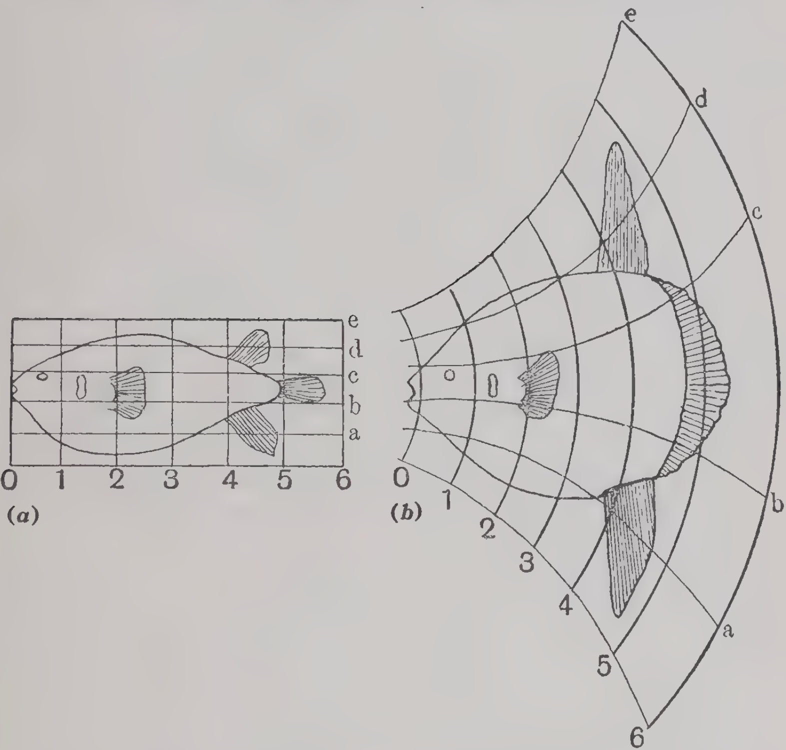

FIG. 27.—Differences in proportions may completely alter appearances. (*a*) Diodon; (*b*) Mola. (From D'Arcy Thompson, Cambridge University Press.)

rates of growth of the regions in question. This may readily be seen in the case of some fish, Diodon and Mola for example, or the neck of the giraffe. Some species, therefore, appear to differ only in their relative proportions.

In some cases the differences between the two sexes of a species may be due to varied rates of growth leading to differences of proportion of certain regions. In crabs the

female has a broader abdomen than the male. During development, in the female the relative breadth of the abdomen (as compared with body length or carapace width) increases as the animal grows larger. That is to say, that the rate of growth in breadth of the abdomen is higher than the rates of growth in other directions and of other organs and that the larger the crab is the broader her abdomen will be in proportion. In the male, after a short period of relative increase, the relative breadth of the abdomen remains constant. In this case the abdomen is growing broader no faster than the rest of the body, and it is consequently narrower in the adult male than in the female.

To sum up, the investigation into the rate of growth shows that young tissues grow faster than old ones, which grow little or not at all; and that all tissues do not grow at the same rate or in all directions.

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CHAPTER XIII

GROWTH, DIFFERENTIATION AND AGE

In the foregoing description of various instances of development, regeneration, asexual reproduction and abnormal growths, the word "embryonic" has been used to a certain extent, without specifying its meaning any more than to say that it is the condition characteristic of the tissues and cells of an embryo, that is to say, of a growing organism. It becomes necessary to enquire further into the meaning of the term, into the properties of growing cells and the relations which growth bears to differentiation and cell division.

The ovum may be said to possess a certain amount of differentiation since usually it is very large (for a cell at any rate), contains quantities of nutritive materials and is not capable of further development without a suitable stimulus of activation. The cells produced by the division of the ovum are free from these hindrances; they are more wieldy in size, there is a larger ratio of nuclear size to cell size than in the ovum, and, except for those of the lower pole, they divide and grow rapidly. It is the large size of the cells of the lower pole, due to their large content of yolk, which is responsible for their restricted activity. All animals and plants, therefore, start growing from a condition in which the cells are simple, rich in protoplasm and unencumbered with any other structures. The greatest part of the plant is formed by the growing point, the frog grows in length by the activity of the rim of the blastopore, the worm elongates by a growth zone in front of the last segment.

The cells of these zones are in this undifferentiated condition, which is also termed embryonic.

In regeneration it has been shown that the preliminary to the growth of the new part is the formation of a bud of small cells, rich in protoplasm and without differentiation. These cells may be derived from differentiated tissue cells by dedifferentiation, or from cells which have up till then remained embryonic. Similarly, in asexual reproduction, new individuals arise from embryonic cells. Whether they be undifferentiated cells of Hydra, dedifferentiated epidermal cells of the leaf of the Begonia or cells produced by a divided ovum, all growing tissues have in common the fact that they are undifferentiated.

It might be objected that since asexual reproduction and the formation of callus and galls in plants from formed tissues (i.e. tissues other than the growing point or the cambium) are of such common occurrence, there can be little truth in the statement that growing tissues are undifferentiated. But in plants the protoplasm itself remains relatively undifferentiated; it is the production of the cell wall, really outside the cell, that constitutes differentiation. Consequently, if the protoplasm within the wall be stimulated to divide, the result is a number of smaller cells without specialized cell walls and which have dedifferentiated by the very fact of their having divided. The bud on the leaf of the Begonia illustrates this. Without the stimuli which are at work in regeneration, gall formation, etc., the cell does not normally divide any more when its wall is thickened, so that it is legitimate to speak of such a cell as being more differentiated than a cell of a growing point for instance.

Differentiation sets in in the young organism soon after the beginning of development, at about the time when the curves for the rate of growth show a decrease. In fact, the rate of growth appears to vary inversely as the state of differentiation. In regeneration and asexual reproduction there are the same relations between growth rate and

differentiation. In tumours the rate of growth is highest in those whose cells are the least differentiated and the most embryonic. Benign tumours, i.e. those which maintain a certain amount of differentiation, lose their differentiation when grown in vitro and grow rapidly.

It looks, then, as if differentiation prevented cells from growing, and this is corroborated by the evidence from tissue culture, where, when two tissues are cultured together, they remain differentiated and grow little, whereas when only one is cultured it dedifferentiates and grows fast. Owing to the factors, such as the surface volume ratio, which tend to keep cell size constant, true growth must take place by cell multiplication. This is achieved by the well-defined process of cell division whereby the contents of a cell are divided between its two daughter cells. This will present no difficulties if the contents of the cell are of a fluid and formless nature. But if the cell is differentiated it contains various formed structures, such as muscle fibres, elastic or skeletal matter, which cannot easily be partitioned. The presence of the inert mass of yolk delays the division of the cells that contain it. It is not surprising, then, that the presence of inert substances with which a state of differentiation is usually accompanied should arrest cell division and growth. Those tissues which are capable of physiological regeneration, such as the skin, the blood corpuscles, etc., are not highly differentiated.

Since the organism becomes more and more differentiated as it grows older, it would be expected that regeneration and asexual reproduction would occur more often and more easily in young organisms than in old ones. This actually is the case and in some forms regeneration which cannot take place in the adult can occur in the larval condition. An example of this is the frog, which cannot regenerate a limb, a performance which is perfectly possible for the tadpole. Asexual reproduction does not occur in the adults of the highest group of the Animal Kingdom, the mammals. In these the embryos of armadilloes and sometimes of man are

capable of undergoing division at a very early stage, giving rise to twins. This is comparable to regeneration since each half has to make up that in which it is deficient.

The evidence from tissue culture fits in with these observations, for cultures of tissues from young animals grow well, those from adults only sparsely.

The significance of these instances is obvious, for the young individual is less differentiated than the adult, and similarly animals which are high up in the scale of evolution, having achieved a greater degree of structural complication, are more differentiated than the more lowly forms.

As organisms grow older there is a general decrease of vital activities. The rate of metabolism is lowered. This has been shown to be the case by experimental methods for a large number of forms. A measure of the rate of vital activity is the amount of oxygen consumed, which corresponds to the amount of carbonic acid gas given off by the tissues, and this is relatively greater in young organisms than in old ones. Similarly, the proportional quantities of nourishment and oxygen required by the mammalian embryo developing in the uterus are larger than those necessary for the adult.

Accompanying differentiation there is, therefore, a decrease in the rate of growth and a decrease in the activities of metabolism. This latter can also be referred to differentiation since an embryonic cell rich in protoplasm will have a higher metabolic rate than if it were encumbered with inert matter.

After growth has ceased and the adult animal is living without increasing in size, changes set in which result in senescence, senile decay and finally death. These changes are really nothing more than the continuation of the processes which had been operating during development, viz., decrease in metabolic rate. In old age this is reflected in the lessened power of repair. The damage of wear and tear must be made up if life is to continue; when the constructive processes are no longer able to keep the ascendency

over the destructive ones, life must cease. The accumulation of inert substances in the cells impedes their rate of metabolism and there is no energy for cell division; consequently worn-out tissues are not replaced.

It is possible now to draw a distinction between young and old organisms and give meaning to the terms embryonic and differentiated. Young organisms are those whose cells and tissues are not highly differentiated and therefore are capable of growth; their growth is rapid and their rate of metabolism high. Old organisms are opposite in all these respects.

It is not easy to speak of the age of a plant because different parts have different ages. The formed tissues are more or less senile, or even dead (like the central wood of a large tree), whereas the growing point is permanently embryonic.

The sequence of events through growth and maturity to decay is a continuous process; and therefore senescence or growing old is a continuation and result of development. If by any means the process in any animal is reversed, the tissues will return to a more embryonic condition and the operation will have resulted in rejuvenation. This has actually been done in some cases. Under conditions of starvation Planaria (a flat-worm) will decrease in size, from a length of 25 mm. to 6 or 7. This reduction is accompanied by a certain amount of dedifferentiation, with the result that the reduced organism has the same rate of metabolism as a young Planaria of equal size developing from the ovum. True rejuvenescence has occurred, the reversal of senescence. The rejuvenated animal not only looks young but is young, for young is as young does, and not as the time which it has lived. Such a rejuvenated animal will grow into the adult condition on being fed. The process of rejuvenation can be repeated and in this manner a Planaria has been made to live for a period about twenty times longer than the ordinary length of its life.

The Planarians are lowly animals and it would be

impossible to bring about rejuvenescence in higher forms, such as man, by the simple expedient of starvation. The greater specialization of form and function in the higher animals entails constancy of conditions with delicately adjusted regulatory mechanisms. Temperature of the body, degree of alkalinity of the blood, etc., are carefully regulated, and starvation would merely throw the machinery out of gear, apart from the fact that the presence of a solid skeleton would prevent the possibility of reduction. Rejuvenation can, however, be obtained even in man as a result of stimulation of certain secretions (hormones) and ductless glands. A stimulation of the gland of the reproductive organs can be obtained either by implanting a new gland, or by severing the duct of the gland already present in the body. The effect of this is an increase in metabolic rate and in vitality, which may be very marked indeed. The manner in which the secretion of the reproductive gland produces this effect is not well known, but it is probable that it is exerted through other glands such as the thyroid and the pituitary. For rejuvenation to be successful, all the parts of the body must be affected and to the same extent, or disharmonies will ensue.

In Protozoa the occurrence of conjugation or sexual connexion between individuals has been interpreted as due to the necessity for rejuvenescence. "Old" cultures will not reproduce, and the stimulus from conjugation has been supposed to restore the capacity for division and growth. But the slipper animal (Paramœcium) has been kept for over five thousand generations, produced by ordinary division without conjugation having occurred once. The animals, however, underwent periods of "depression," during which they did not divide and could be regarded as senile. This condition was overcome by a process of internal reorganization (termed *endomyxis*), resulting in reduction and disappearance of certain structures (the large nucleus, for example) and their subsequent replacement. This renewal, which is really a case of physiological regeneration,

The effect of stimulation of the genital gland in producing Rejuvenation in a dog. (From Sand.)

FIG. 28.—Before the operation (vasectomy).

FIG. 29.—After the operation.

produces rejuvenescence, and the animals are then able to resume their capacity for rapid growth and reproduction.

Rejuvenescence is, therefore, an increase in rate of the processes of metabolism.

Age, which is an estimation of the degree of development of an organism, is usually measured in units of time. In the majority of cases this answers fairly well, since each species has its characteristic tempo at which life runs. The assumption of the privileges and responsibilities of citizenship finds most men at the age of twenty-one years in more or less similar conditions of physical and mental development. But age can really only be estimated by the physiological condition of the animal. A rejuvenated Planaria in its twentieth " life " is in the same condition and has the same capacities as one which has just hatched, though the difference between them counted in units of time is great. The tempo of development in all individuals of a species is not identical, and in some pathological cases may be thrown very seriously out of gear. In a disease characterized by extremely precocious " old age," and known as progeria, a man of seventeen may be more senile and decrepid than a normal person of over eighty. This case, again, shows that the age and degree of development of a person cannot be accurately measured by the number of times the earth has revolved round the sun.

Differentiation is, therefore, one of the causes of old age. It has already been shown that this word really covers two things, complications of shape and complication of cells. Now, as to the manner in which differentiation is brought about, it is found that some organs will differentiate on their own account and by themselves, others will only do so when some other tissue is present. The former are called self-differentiating and the latter dependent-differentiating. Self-differentiation is characteristic of the organs which arise early in development. Such, for example, are the limb rudiments, and accordingly it is possible to grow a limb by itself in suitable artificial circumstances, and it will differ-

entiate, up to a certain stage. There comes a time when function is necessary for the successful completion of development and differentiation. For example, the general plan of the blood-vessels is laid down, but their further development is conditioned by the functional requirements of the tissues.

The action of neighbouring tissues in producing dependent differentiation is well seen in the case of the lens of the eye in vertebrates. The eyeball grows out from the brain towards the skin, and at that point the epidermis thickens and differentiates into a lens which sinks into its place in the eyeball. The lens does not develop in the absence of an eyeball, and if an eyeball be grafted elsewhere under the skin, a lens will be formed there. The eyeball therefore stimulates the epidermis to differentiate into a lens. This is comparable to the differentiations induced in undifferentiated tissues in vitro by connective tissue. Recent work has shown that the formation of the nerve cord and the general morphological differentiation of the frog embryo is dependent on the cells situated on the dorsal edge of the lip of overgrowth surrounding the blastopore. This region, since it "organizes" the development, has been called the *Organizator*. Other examples of the action of one tissue upon another are to be found in regeneration. The sense organs of taste on the barbels of fish do not regenerate in the absence of the nerve; in the earth-worm the nerve cord must come right up to the surface of amputation for regeneration of a head or a tail to occur.

Function may have an important bearing on growth. The nerve cells of the cerebellum of the brain do not attain their full size unless the limbs with which they are connected are functional. Artificially raising the pressure of the fluid in the bladder of a mammal causes the wall of the bladder to thicken greatly and also brings about the differentiation of striated muscle therein; the muscle fibres of a normal bladder are smooth. By means of its artificially produced striated muscle the bladder pulsates, an action obviously

adapted to diminish the pressure within the bladder by expelling the fluid. Dogs which through deformity or accident possess no front legs are necessarily bipedal, and the change in function occasioned by the novel mode of progression entails marked modifications of the growth of the bones and muscles of the hind legs. The alimentary canals of frogs are longer than is normally the case when they are fed on plant food, those of birds can be made to grow thicker on diets of grain.

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CHAPTER XIV

GROWING SMALLER, AND THE CAUSES WHICH PREVENT ORGANISMS FROM GROWING LARGER

The processes of growth and differentiation which have been considered in the preceding chapters all work in one direction, making for increase in size and in complication of shape. It may be asked whether it is possible for these processes to be reversed and for organisms to decrease in size and in complexity. The answer is that they can, and some cases of " degrowth " or reduction and dedifferentiation will now be considered.

It is no use to look for cases of reduction in the higher animals where the degree of specialization which has been reached entails the possession of a firm skeleton and a fixed size. There may, however, be atrophy of certain parts when their function is over, which results in their degrowth. The Ascidians or sea-squirts are a group of degenerate animals related to the lowest vertebrates. Many of them are colonial, and in Clavellina the several individuals or zooids are all connected together at their base by a common tube or stolon. When placed in unfavourable surroundings, such as impure water, a zooid of Clavellina loses its organization completely, and from a creature with alimentary canal, nervous, excretory, respiratory, circulatory and reproductive systems, it becomes a small white mass of cells irregularly arranged round a few contained and closed cavities. Dedifferentiation has taken place and to an astonishing degree, for none of the organs or tissues of the original zooid can any longer be recognized. This process is, of course, the reverse of differentiation and consists in the loss of those charac-

teristics which distinguish differentiated cells. At the same time there has been a great decrease in size, yet the resulting object is just as alive as was the fully-developed zooid. This shapeless mass of cells is capable of redifferentiating and growing to form an adult Clavellina, which will, however, be smaller than before the operation.

Perophora is another colonial Ascidian related to Clavellina, and, like it, consisting of zooids and stolon. If a piece of stolon with a zooid be placed in impure sea water, the zooid will dedifferentiate and be resorbed into the stolon, because for reasons which will be given later the stolon is not so adversely affected by the unfavourable conditions as is the zooid. On the other hand, the zooid has a greater power of acclimatization to slightly unfavourable surroundings. In such conditions the stolon will be reduced and be resorbed into the zooid. In Perophora, therefore, reduction of the one or of the other portion can be produced according to circumstances.

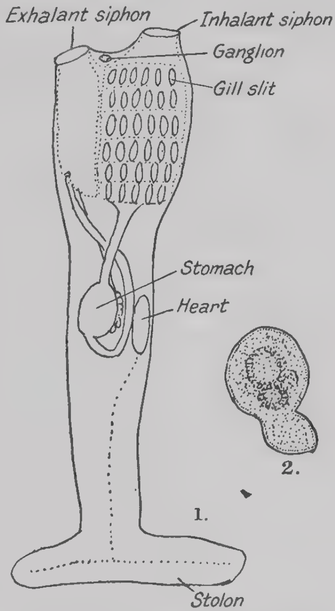


FIG. 30.—The normal (1), and reduced (2), conditions of the Sea Squirt (Clavellina). (From Huxley, *School Science Review*.)

The hydroid polyps, such as Obelia, consist of a stem bearing numerous zooids. In bad conditions these zooids lose their differentiation and are resorbed into the stem in a manner comparable to the resorption of the zooid into the stolon of Perophora.

Tissues have different powers of resistance to adverse conditions according as to whether they are differentiated or embryonic. Differentiation requires an expenditure of energy in maintaining the cell in its differentiated condi-

tion. In adverse conditions, such as the presence of poisons, the cells cannot expend this energy and therefore cannot keep up their differentiation. Consequently, the zooids of Clavellina, Perophora or Obelia dedifferentiate under these circumstances. The less differentiated stolons, on the other hand, are much less affected, with the result that the zooids are resorbed into the stolons. But differentiated tissues have a greater power of acclimatization to adverse conditions up to a certain point. Consequently, dilute concentrations

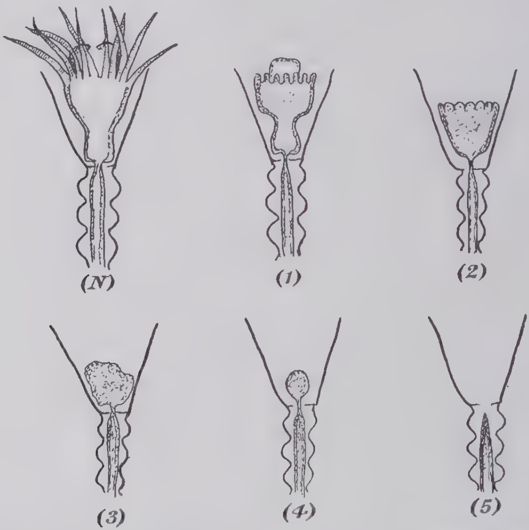
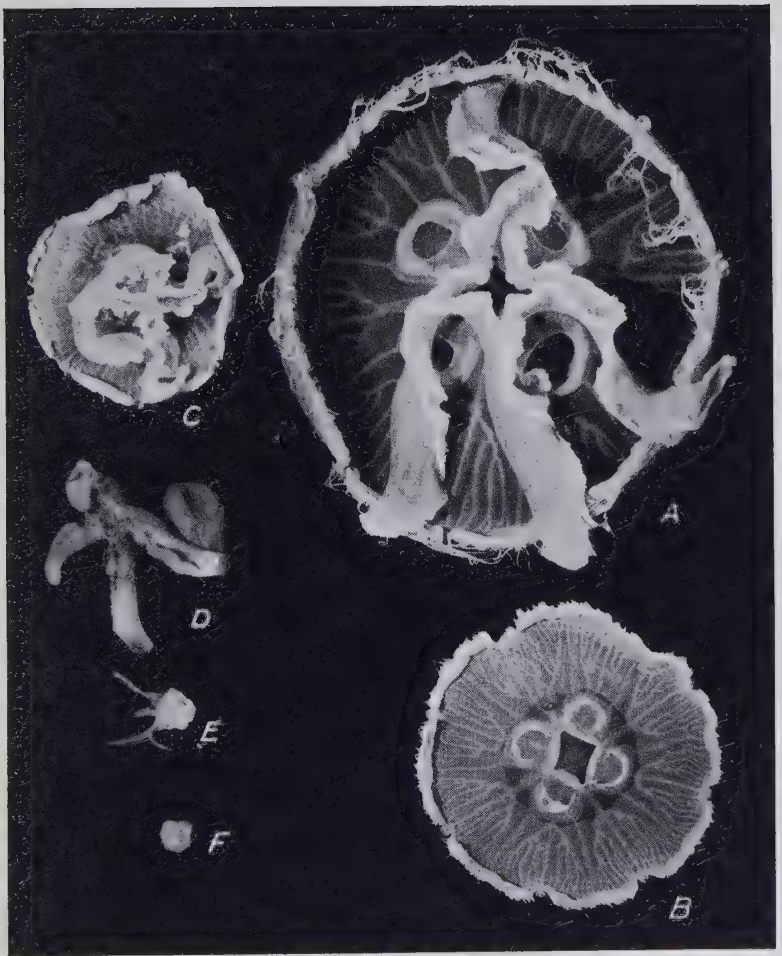


Fig. 31.—Normal (*N*) and five stages (1–5) in the resorption and dedifferentiation of Obelia. A case of "degrowth."

of poisons which affect young organisms are overcome by older ones; and in the case of Perophora the less differentiated stolon is resorbed into the zooid.

Starvation will also produce reduction. Under such circumstances the jelly-fish Aurelia decreases in size and also changes its shape, becoming more spherical. Starvation of the flat-worm Planaria leads to most interesting results, for although the size of the animal decreases its relative proportions and shape remain the same.

This last case leads on to the consideration of how the



[From de Beer and Huxley, *Q. J. Micr. Sci.*

FIG. 32.—*A* and *B*, normal jelly-fish (Aurelia); *C* to *F*, different stages of reduction and dedifferentiation.

form of an organism is maintained, a process known as regulation. It is obvious that something is at work in the starving Planarian to regulate its form.

The tendency of all protoplasm is to produce a specific form and definite shape—that of the adult of its species—under normal conditions. This is achieved by an orderly sequence of consequential processes, each step being determined by preceding ones and determining the next. There are as many different kinds of protoplasm as there are species of living organisms, and each has its own tendency with its own specific form. Under normal circumstances these processes succeed one another regularly and by growth and differentiation give rise to the adult. But if the circumstances be changed, the results will be changed also, and as in the cases which have been described in this chapter, reduction and dedifferentiation may occur.

Even normal development is not solely a process of growth and differentiation. In the frog it was seen that at metamorphosis while certain organs grew, others, notably the intestines, gills and the tail, were reduced, the last two completely. This differential growth and degrowth of parts is of common occurrence in the animal kingdom. The sea-squirt starts life as a "tadpole," which later loses its tail. The larvæ of sea-urchins and starfish undergo a metamorphosis whereby the rudiment of the adult develops within the larva, and at the expense of the other structures of the larva which are resorbed. In almost all species which are in advanced stages of parasitism the passage from the larval into the adult condition is accompanied by profound changes usually described as degenerative but consisting largely of dedifferentiation and reduction of certain parts.

Upon a return to normal conditions in many cases an organism will return to its former structure. This has been seen to occur in Clavellina and it has been observed in certain hydroid polyps. Sea-urchin larvæ may be made by dilute poisons to dedifferentiate into little round balls and to reduce their skeleton, but on return to normal sea water they

redifferentiate. Regulation therefore does its work " other things being equal."

When two Hydras of different sizes are grafted together a regulation of size will take place so that the larger member will shrink and the smaller grow, until, when both are equal in size, they separate. Here there appears to be a balance between the two organisms which tends towards an equilibrium. A balance has already been shown in the case of Perophora, where the stolon is normally balanced with the zooid, but where the equilibrium may be tilted to one side or to the other according to external circumstances.

In animals the loss of one member of a paired organ is compensated by increase in size of the remaining one. Thus, if one kidney be removed, the other will grow larger. All these cases suggest the idea of a balance between different parts, so that something affecting one part brings about a change in another.

Mention must be made of a particular process which affects the growth of an organism and causes it to divide, in other words, to twin. In the higher animals, including man, this process takes place very early in the life-cycle. Its effect is the more or less complete division of the rudiment of the embryo into two by longitudinal fission. If the fission is complete two normal twins may result, and by repetition of the process, four, as in the Armadillo, all derived from one fertilized ovum. If the fission is incomplete monsters will be produced with two heads or two tails. But in any case it is to be observed that the products of fission of the original embryo each have their own regulation and grow as if they were normal single organisms as far as circumstances and their degree of fission permit.

Except for those species in which twinning occurs, one ovum gives rise to one individual. Each cell at the two-cell stage will form a half of the individual, at the four-cell stage each cell will be responsible for the formation of a quarter. If, however, one cell from these or later stages be separated from the rest, in a developing sea-urchin it will develop into

a complete larva, though of smaller size. Normally this particular cell would only have produced a part of an organism; when detached it is regulated to produce a complete organism. In nature this process may be seen in those species of hymenopterous insects in which *polyembryony* occurs. This consists in repeated division of the ovum into several cells which separate, and each of which produces a complete insect.

Regulation is therefore a process or complex of processes which, in accordance with circumstances both internal and external, tends to produce and maintain a definite form. When it is allowed to proceed normally, normal results are obtained. On the other hand, when conditions are altered, as in the case of the frog's egg implanted in the body (described in Chapter VII), regulation is upset and great abnormality results, varying from imperfect attempts to form an embryo, to masses of undifferentiated tissue invading the host and resembling malignant tumours.

One of the most important problems in developmental mechanics deals with the cessation of growth when the organism arrives at maturity. During development the organism is increasing in size. Why does this process stop? Stated in these terms the problem is principally concerned with animals, for plants as a rule go on growing as long as they live by means of their growing points. But even in plants there are restrictions in growth.

A case of this may be seen in the buds of a stem close to the growing point. These buds are formed in the angles between the leaves and the stem, but they are prevented from developing, in some manner, by the growing point. It is only when the growing point has got a sufficient distance away from any bud that it will develop. This can be tested experimentally, for if the growing point be rendered inert by covering it with a cap of gypsum the buds beneath it will develop. The same result is obtained when the growing point is killed. If, however, the gypsum cap be removed, the growing point will resume its growth and the shoots

which have developed from the buds during its enforced quiescence will die. The growing point obviously exerts an influence which suppresses the growth activities of the buds of the stem immediately beneath it, and its power is greater than those of the growing points of the minor shoots, which die. If, however, these minor shoots are allowed to grow until they are about three times as long as the apical shoot before the gypsum cap is removed, the latter is killed. In this case the inhibiting power has been usurped by the minor shoots.

The growing point is the region of highest metabolic rate in a plant. From the growing point of the stem downwards (and from that of the root upwards) there is a gradual decrease in the rate of metabolism of the tissues. This change in rate from place to place along the long axis of the plant is known as an *Axial Gradient* of Metabolic rate. The inhibitory action of the growing point is also described as the physiological dominance of a region of high metabolic rate. The dominant region is regarded as controlling the other regions, which are subordinate to it, within a certain range which is the range of dominance. It is only when the growing point reaches a sufficient distance away from any particular bud that the latter is freed from the range of dominance and grows on its own. In this manner the region of dominance moves up the stem, like a tune transposed up the keys. It is impossible to localize it in any particular spot since it is always changing, and dominance must be considered as the property of the whole mass of embryonic tissue of the growing point.

The range of dominance can be decreased by conditions which curtail vital activities and decrease metabolic rate. It has already been described how a gypsum cap stops growth and decreases the range of dominance. A similar effect is obtained when the tissues between the growing point and the bud are subjected to cold or to an anæsthetic. This looks, therefore, as if dominance were something conveyed by the living tissue, like a nerve stimulus.

In animals axial gradients have been demonstrated in most groups. The methods usually employed for this purpose are three: (i) the metabolic rate can be measured directly by

measuring the amounts of carbon dioxide given off by the tissues ; (ii) when the organism is placed in a poison of above a certain strength, the region of highest metabolic rate disintegrates first ; (iii) if the poison is very dilute and below the power of acclimatization of the tissues, the region of highest metabolic rate disintegrates last. By all three methods it is consistently found that the region of highest metabolic rate in an animal is the head, and that an axial gradient exists from the head to the tail.

Animals do not grow indefinitely, and for the lower animals at least it appears that the limit of size and of growth coincides with the range of dominance of the head region. *Planaria dorotocephala* habitually reproduces asexually by transverse division. The posterior portion of the animal, freed from the dominance of the head, detaches itself and grows. In the process it has established a dominant region of its own. If, however, the range of dominance of the head of the whole worm be increased, as it can by stimulating the head, the posterior portion is brought back within its influence and detachment does not take place. The particular activities of the posterior portion are inhibited by the dominant region. The range of dominance of the head may be decreased (by poisons, or by cutting off the head), in which case the posterior portion achieves its independence all the sooner.

For the establishment of a new region of dominance, this region must in some way be isolated from the main dominant region. This isolation may be physiological, as in the case of Planaria, when the posterior portion sets up a dominant region of its own before detachment. Or isolation may be physical, as in the small pieces into which Ctenodrilus and Procerastea break up, and which thereupon grow. The isolation of cells of divided ova of sea-urchins enables these cells to acquire dominant regions of their own which regulate the growth and development into perfect larvæ.

The adult form in animals must be regarded as a figure of equilibrium between the protoplasm with its hereditary qualities and the environmental forces. It contains a dominant region whose function it is to keep down the banners of revolt

which other tissues might set up by growing on their own account. If a portion of the form be removed, the equilibrium figure will be restored by regeneration of the missing part (where possible), which ceases growing when regeneration is complete. Regeneration, then, is growth within the range of dominance. All other growth after the adult stage is reached can only be done if the growing tissue is isolated from the dominant region. This means that other centres of dominance are established, and consequently other individualities. These new individualities may manifest themselves as new individuals, produced by asexual reproduction ; or as tumours, which appear to have an individuality of their own. Tissues which in the organism are incapable of even physiological regeneration can be made to grow indefinitely in vitro, under which condition they are released from the dominance of the organism and lose their differentiation.

In animals the dominant region is the most differentiated in the whole body, the head and in particular the brain and the nervous system. But this differentiation has as its essential effect the perfection of methods of conveying stimuli over the range of dominance. In plants, on the other hand, the dominant region is the most embryonic. In plants, therefore, the dominant region is always growing, but it always grows in the same manner, making additions to the plant similar to those which have already been made.

In colonial animals growing by means of a stolon the individuals or zooids each have a dominant region with a certain range of dominance. The stolon, therefore, cannot grow a new individual until it has passed out of this range. This will account for the more or less regular equidistant spacing of zooids arising from a common stem or stolon.

Normally, the zooid is dominant over the stolon in these forms. But under certain circumstances the dominance may be reversed, as when in Perophora the zooid is resorbed into the stolon under adverse circumstances. In a healthy animal none of the tissues are dominant over the head region, but should some of these tissues become cancerous they develop a dominant region of their own, which, growing rapidly at a

high metabolic rate, may place the rest of the organism in subordination to it.

No satisfactory explanation has yet been given of physiological dominance, and how it is that one region can curtail the activities of others at a distance and regulate the form of the organism. For the moment physiological dominance must remain a working hypothesis of great value.

Growth of particular regions may be arrested by a deficiency in food supply. When a female rat with a tumour becomes pregnant, the tumour ceases to grow while the embryo develops. After birth the tumour resumes its growth.

Another factor restricting growth is the state of differentiation of the tissues. Several facts relating to this have already been dealt with. First, there is the fact that growth when it does occur takes place from undifferentiated cells. When dedifferentiation is produced, as of a benign tumour cultivated in vitro, growth is accelerated ; undifferentiated tumours grow faster than differentiated ones ; only the least differentiated tissues of the body are capable of physiological regeneration. The factors producing differentiation therefore at the same time tend to restrict growth, and these factors are referable to the action of one tissue on another, as has been shown to be the case in the dependent differentiation of the lens of the eye, and in tissue culture, and differentiated cells will not divide.

Lastly, mention must be made of substances which definitely inhibit growth, and therefore act antagonistically to the growth-promoting substances obtained from embryos and from autolysed tissues. This growth-stopping substance increases in amount with age.

The causes which limit growth may therefore be referred to the fall in rate of vital activities consequent on differentiation, the restricting action of a process called dominance and the effects of a growth-stopping substance.

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CHAPTER XV

INORGANIC ANALOGIES WITH GROWTH

It is natural when reviewing the various phenomena of Growth in organisms to enquire whether anything comparable is to be found in inorganic nature. The behaviour of crystals at once suggests itself to anyone who has dealt with them. Crystals are the figures with symmetrical shapes, bounded by plane surfaces which are formed by various substances when they solidify from a liquid or gaseous condition. A familiar example is to be found in the crystals of water which make up snowflakes. There are various standard types of crystalline structure, and each substance conforms to its particular type (or types, for some substances may crystallize in more than one form) with rigorous specificity. As more and more of the substance solidifies from solution, the crystals grow, increasing in size and in weight. A crystal may, moreover, grow by the addition to itself of a substance different from that which first formed it, provided that the second substance crystallizes in the same form as the first. In this manner crystals may be formed consisting of one substance in the centre and another on the exterior. Further, if a crystal be injured by having a portion of itself removed, it will resume the form characteristic for the crystals of its substance, and in this way may be said to regenerate.

The process of crystal formation, however, has really nothing in common with growth of living organisms. For the growth of a crystal it is necessary that it be in the presence of more of its identical substance, or of a sub-

stance with identical mode of crystal formation. The organism grows by assimilation and conversion of substances (more than one) totally different from itself. For the crystal the solution must be fairly concentrated, for the organism the concentration of food substances may be dilute. The crystal grows by regular additions of similar particles in regular places on the surface: the organism absorbs its food and builds it up by metabolism throughout its body. The analogy of the behaviour of a crystal with growth need not be pressed any further. In spite of the sensational properties of certain kinds of crystals, such as of being "liquid," or capable of rearranging their internal structure, their behaviour furnishes an interesting but false analogy with the growth of organisms.

Artificial "organisms" have been made to grow by various methods. By dissolving a substance in a volatile liquid, subjecting the solution to capillary attraction so that it climbs up a string, and then evaporating the solvent, the solute can be made to form curious arborescent structures of which "nitrophenol trees" are an example. By placing pills of particular substances in certain liquids osmotic effects can be produced, which cause the pill to swell up and burst out. The process then begins again and by a succession of osmotic expansions, supposedly lifelike growths result. Precipitation of salts in certain circumstances produces growth-like forms, and the action of certain minerals produced a structure which for a long time was held to be a fossil organism and termed *Eozoon canadense*.

What these experiments show is that increase in size can be produced by ordinary physical forces like osmotic pressure, a fact which can also be derived from the direct study of organisms. Attempts to find analogies of this kind are interesting, for they give ideas of how living effects might be produced by simple inorganic forces, but their results lack the most important characteristics of organic growths, viz., metabolism, the conversion of foreign sub-

stance into the growing matter, and its subsequent breakdown and decomposition.

It must be admitted that the manifestations of life in organisms take place by means of physical and chemical actions and reactions. For whatever protoplasm may be, it is composed of atoms and molecules which must behave according to the established principles of physics and chemistry. Metabolism itself consists of innumerable such actions and reactions. The fact that the principle of conservation of energy holds good for organisms as well as for inorganic matter opens the way for a series of highly instructive quantitative investigations, and it is found to be possible to compare the reactions of protoplasm with the reactions of inorganic substances under various conditions.

It is well known that in most physical and chemical reactions the rate of the reaction is accelerated by a rise in temperature. Temperature has been found to have a precisely similar effect on growth of protoplasm. It is possible to determine a temperature coefficient of growth and to calculate the amount of acceleration which a certain rise of temperature will produce, and these values approximate closely to those obtained by experiment.

Facts such as these suggest that the processes active in growth are physical and chemical reactions obeying laws already familiar in the inorganic universe, though the difficulties in unravelling these reactions are very great on account of their complexity. In the process of phagocytosis, for example (the action of ingestion of foreign and decomposing substances by the white corpuscles of the blood, which is one of the main lines of defence against infection), four different reactions have been disentangled, each with its own temperature coefficient; and the number of reactions present must be very much greater than four.

A *catalyst* is a substance which produces acceleration or retardation in a reaction while it remains unchanged at the end of the reaction; things very similar to them have already been met with as ferments or hormones. Cata-

lysts are of frequent occurrence in chemical reactions, and in organisms the actions of enzymes are comparable to those of catalysts. For example, the presence of manganese dioxide accelerates the liberation of oxygen from potassium chlorate. But in the case of the action of pure nitric acid on copper, one of the products of the reaction is itself the catalyst, viz., oxides of nitrogen, so that the acceleration of the rate of reaction itself increases. This is like the principle of the rolling snowball; as the ball rolls it gets larger, and the larger it is the more snow it picks up. Such a reaction is termed autocatalytic, and given infinite supplies of the reacting substances the rate of the reaction will increase until it is infinite. Another way of expressing this is to say that it obeys the law of compound interest, the bigger a sum of money gets, the faster will it get still bigger. Represented graphically, a curve showing the amount of substance transformed by an autocatalytic reaction (mass plotted against time) will at first rise slowly, then faster and faster still until it becomes vertical. In practice, however, the supply of reacting substances is not infinite but limited, and as the supply decreases there comes a time when the amount of substance transformed decreased also. Together with the decrease in amount of substance transformed in a given time, the rate of the reaction falls off, until it ceases altogether when the supply of substance is exhausted. The curve for such a reaction is S-shaped, rising at first slowly, then faster and gradually tailing off to the horizontal again (mass plotted against time).

The shape of this sigmoid curve will immediately suggest that obtained by plotting the increase in size and weight, in other words, the growth of an organism, against time. The shapes of the curves are similar. The volume of an organism increases at first slowly, then faster, and lastly slowly again until, when the adult condition has been reached, growth ceases. Regeneration is similar. Can growth then be an autocatalytic reaction?

The curves of the growth of an organism and of an autocatalytic reaction do not tail off horizontally for the same reason. The latter reaction ceases because of lack of supply and accumulation of the products of the reaction. The former must stop for a different reason since not only is supply kept up in the form of food, but waste products are excreted, so that they cannot possibly "clog" the reaction. The rate of growth ceases because of the processes of regulation and differentiation.

The latter portions of the two curves then owe their similarity to different and unconnected reasons. It remains to be considered whether the first portions may not correspond. The early increase in size of animals and plants follow the compound interest law, the rate of production increases with the amount which has been produced. The production of new nuclear matter during division of the ovum is a process of this nature; the pollen tube grows faster as it grows longer. Protoplasm contains certain substances or catalysts which, as has been seen, promote growth. The more protoplasm there is the more of this catalyst there will be.

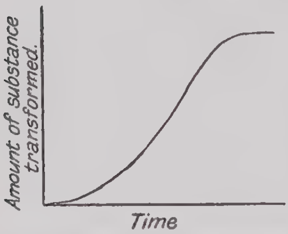

FIG. 33.—Curve of an autocatalytic chemical reaction showing similarity with that shown in Fig. 26 (c).

But it must not be forgotten that growth entails not one reaction but several. Some of these are autocatalytic, others may not be. And in measuring the end results of growth, the increase in size and weight of an organism, only the resultant of the activities of all the reactions is obtained. That is to say, that one is only dealing with the average of all the reactions. It is, therefore, incorrect to say that growth is an autocatalytic reaction; rather, some of the reactions involved in growth are autocatalytic.

Many chemical reactions are reversible. It has already been mentioned that in certain cases protoplasm may cease growing and undergo reduction. Reduction results in

decrease in size, and it may be asked whether growth and reduction may not be the different aspects of one reversible reaction.

An end result may be brought about by certain methods, but an opposite result need not necessarily be caused by opposite methods. A simple example will make this clear. The engines of all motor-cars revolve in a clockwise direction when seen from the front. The ordinary consequence of the working of the engine is the forward movement of the motor-car. But when the car is reversed and goes backwards, the engine is not reversed, it still rotates in the same direction. The end result has been changed by an altogether different mechanism, viz., the insertion of an extra cog-wheel. Growth takes place by cell division, but in reduction the cells do not fuse together again, nor does the organism retrace its steps in development like a cinematograph film run through in the wrong direction. Growth and reduction cannot therefore be regarded as parts of a reversible reaction.

Inorganic analogies, then, while very instructive and illustrative of certain events in the reactions of living matter, are as yet unable to throw much light on Growth itself.

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CHAPTER XVI

CONCLUSIONS

The study of growth has necessitated a certain amount of digression in order to cover the provinces of the processes connected with growth. From this study has emerged the conclusion that true growth is the creation of life. Whether it be in development from the ovum, regeneration, asexual reproduction or abnormal growths, true growth means the production of new living matter. It is no small wonder, therefore, that it has proved difficult to attack and elusive to define ; for the conditions of the activities of living matter are still very imperfectly understood.

It has been found that true growth is a particular case of the relations between the constructive and destructive processes of living matter. Development, regeneration and asexual reproduction are all aspects of this fundamental property of living matter, all carefully regulated and resulting in definite and specific form. When regulation breaks down abnormal growths may result.

Growth is the means by which species cover the earth and subdue her, and it is a powerful weapon. The power of increase of a bacterium from unity to a number of thirty figures in a day indicates the nature of its strength, and when it is said that sometime in the next millenium there will not be standing room on earth, it is the growth and production of new living matter of which these hosts of animals will be composed that will be responsible for so troublesome a state of affairs.

The main structural differences which exist between organisms are the result of different intensities and

directions of growth, for form is a result of growth.

True growth takes place by cell division. If it be granted that the size of the cells of particular tissues does not vary beyond narrow limits, growth cannot occur without cell multiplication. On the other hand, cell multiplication must be accompanied by assimilation of new material or cell size will decrease. Thus growth and cell division during true growth are inseparable. Is one the cause of the other, and if so, which? Or are they both effects of some deeper cause? These questions are difficult to answer, but it is probable that they are both related to one ratio which the size of the nucleus bears to that of the cell.

In plants the growth of the mass may be the primary factor, since form may be modelled before the mass of protoplasm splits up into cells. This has led to the aphorism :—"The plant makes cells, cells do not make the plant." In animals the growth of tissues without cell boundaries (syncytia) furnish an example of growth in which true cell division plays no part. On the whole it may be concluded that the growth of the whole organism is more than the sum of the activities of its constituent parts, and that in true growth cell multiplication is, as a rule, inseparably connected with increase in living matter.

Protoplasm can exist in one of two conditions : embryonic and differentiated. These are only the visible expressions of the forces in virtue of which embryonic tissues grow fast, have a high rate of metabolism and are young, while differentiated tissues grow little, have a low metabolic rate and are old. The condition of the tissue from the point of view of differentiation is of importance in connexion with its power to grow. Typically, all tissues which are freed from a region of dominance will grow as is shown from tissue culture, regeneration, asexual reproduction, etc.; if sufficiently undifferentiated, as an isolated cell from the divided ovum of a sea-urchin, or capable of dedifferentiation, as in the leaf of the Begonia, it will grow to the typical form of the adult of its species. This means that growth is funda-

mental, and stoppage of growth is due to something else added on.

It is unfortunate but true that organisms will not conform to hard and fast definitions, and consequently, since "growth" as defined in a dictionary means increase in size, all processes conducive to this result must be included. But whether it be permanent or temporary, increase in number or in size of cells, by absorption of water or production of new living matter, growth is not different from the other phenomena of life in refusing to be placed in water-tight compartments.

The difficulty in dealing with growth analytically resides in the fact that it is not a thing nor even a process, but several processes involving countless factors. The observed organism only shows the result of these forces, in much the same way as a series of fossil forms illustrates the result of evolution. There is no need to invoke mystical forces to explain results which in the present state of knowledge are not understood. The processes of growth most certainly have their causes, but these causes are not likely to be understood until the chemical and physical properties of living matter have been thoroughly explored. Then it may be that forces will be discovered which have no parallel in inorganic nature, but if they work in an orderly consequential manner (as there is every reason to believe that they do) observation and experiment may still be brought to bear upon them, and they will be capable of analysis.

This in no way commits one to the "materialist" idea of life. Neither does it mean that life is nothing but physics and chemistry. What this point of view does stand for is that whatever the processes of life may be, they work in an orderly way, producing similar effects under similar conditions. Steering between "materialism" and "vitalism," this conception has become known as mechanistic.

Already it is clear that a large number of reactions manifested by life are physical and chemical, and this,

therefore, applies to growth too, since it is only a particular instance of vital activity. Thanks to the development of the experimental method of research, growth is beginning to be susceptible of control by growth-promoting and inhibiting influences, and this power of control is a step towards a complete understanding of the subject.

APPENDIX

A list of references to some recent papers bearing on the subject of this book. The first figure is the volume number, the second the year of publication :

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